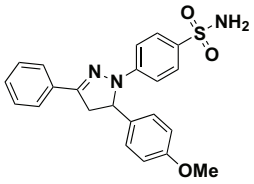
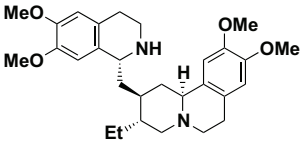
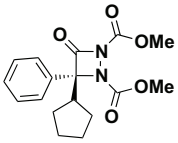


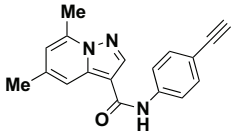
ML141
Cdc42 inhibitor
(*Surviladze et al. 2010*)



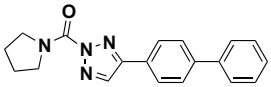
ML081
RBBP9 inhibitor
(*Bachovchin et al., 2009*)



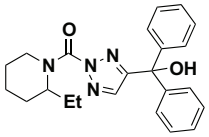
ML174
PME-1 inhibitor
(*Bachovchin et al., 2011*)



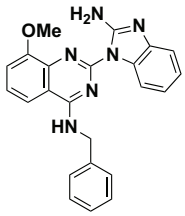
ML198
Activator of GCase
(*Goldin et al., 2012; Rogers et al., 2010*)



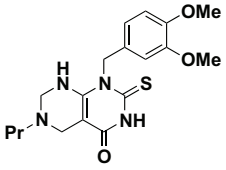
ML225
PAFAH2 inhibitor
(*Adibekian et al. 2010b*)



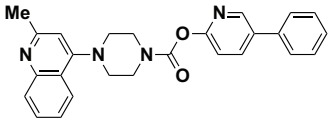
ML226
ABHD11 inhibitor
(*Adibekian et al. 2010a*)



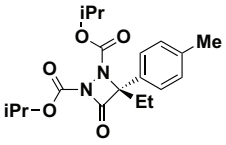
ML240
p97 AAA ATPase inhibitor
(*Chou et al. 2013*)



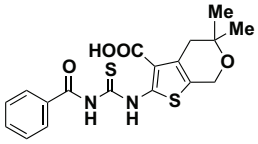
ML247
Non-inhibitory chaperone of acid alpha glucosidase
(*Marugan et al. 2010*)



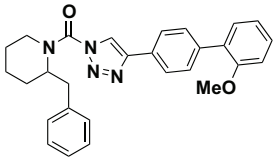
ML256
pPAFAH inhibitor
(*Nagano et al. 2010*)



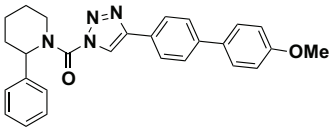
ML257
ABHD10 inhibitor
(*Zuhl et al. 2012*)



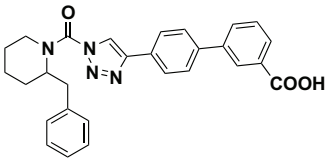
ML282
Rab7 GTPase pan-inhibitor
(*Hong et al. 2010*)



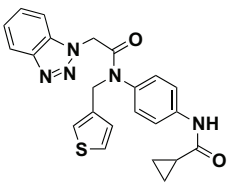
ML294
DAGL-β inhibitor
(*Hsu et al. 2010a*)



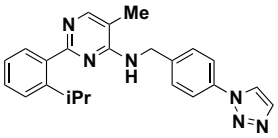
ML295
Brain-penetrant ABHD6 inhibitor
(*Hsu et al. 2010b*)



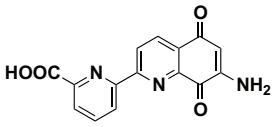
ML296
Peripherally-restricted ABHD6 inhibitor
(*Hsu et al. 2010b*)



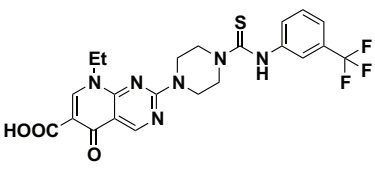
ML300
3CLpro inhibitor
(*Turlington et al. 2010*)



ML323
USP1 inhibitor
(*Liang et al. 2014*)

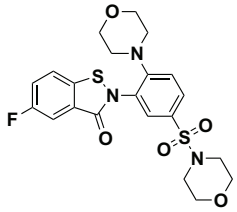


ML325
Pan-PAD inhibitor
(*Dreyton et al. 2014*)

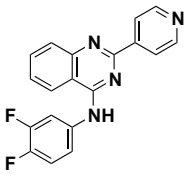


ML328
Dual AddAB/RecBCD inhibitor (*Amundsen et al. 2012*)

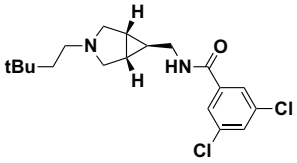
Enzyme modulator Hydrolase



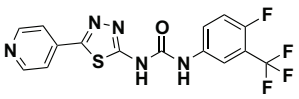
ML345
IDE inhibitor
(*Bannister et al. 2010b)*



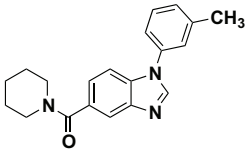
ML367
Inhibitor of ATAD5 stabilization
(*Rohde et al. 2010)*



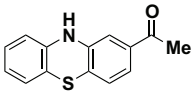
ML218
Cav3 inhibitor
(*Xie et al. 2010)*



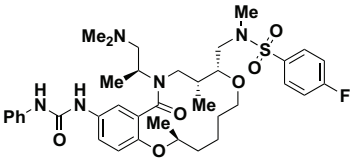
ML216
Bloom helicase inhibitor
(*Nguyen et al. 2013, Rosenthal et al. 2013)*



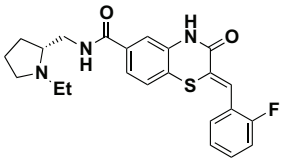
ML148
15-HPGD inhibitor
(*Niesen et al. 2010)*



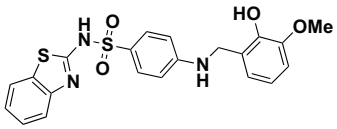
ML171
NOX1 inhibitor
(*Gianni et al. 2010)*



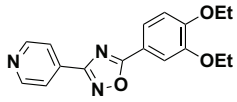
ML238
Inhibitor of P. falciparum bc1 complex (Q1)
(*Heidebrecht et al., 2012; Weiwer et al., 2010)*



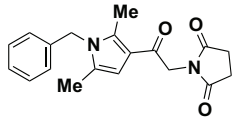
ML276
Pf G6PD inhibitor
(*Preuss et al. 2012)*



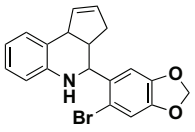
ML355
12-LO inhibitor
(*Luci et al. 2014)*



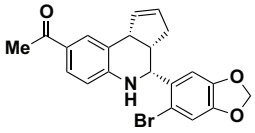
ML007
S1PR1 agonist
(*Gonzalez-Cabrera et al., 2008)*



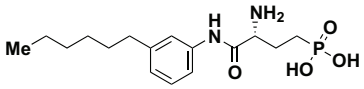
ML031
S1PR2 agonist
(*Satsu et al., 2013)*



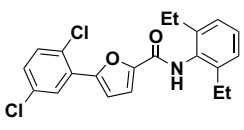
ML050
GPR30 antagonist
(*Bologa et al. 2006, Dennis et al. 2009)*



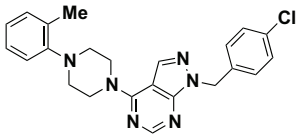
ML051
GPR30 agonist
(*Bologa et al. 2006)*



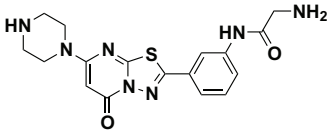
ML056
S1PR1 antagonist
(*Sanna et al., 2006, PDB: 3v2y, 3v2w)*



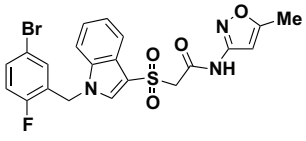
ML131
S1PR4 antagonist
(*Guerrero et al., 2011; Oldstone et al., 2010; Urbano et al., 2011a; Urbano et al., 2011b)*



ML144
GPR35 antagonist
(*Heynen-Genel et al. 2010b)*

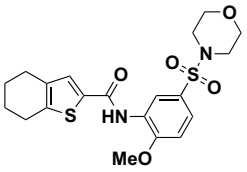


ML165
Integrin $\alpha_{IIb}\beta_3$ receptor antagonist that prevents Mg^{2+} binding (*Jiang et al. 2014, Zhu et al. 2012, PDB: 3t3m)*

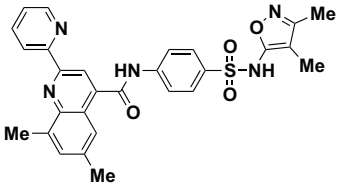


ML169
M1 AChR positive allosteric modulator
(*Bridges et al., 2010; Reid et al., 2011; Tarr et al., 2012)*

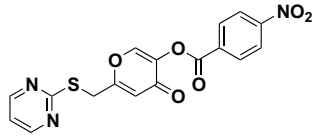
Hydrolase Membrane traffic protein Nucleic acid binding Oxidoreductase Receptor



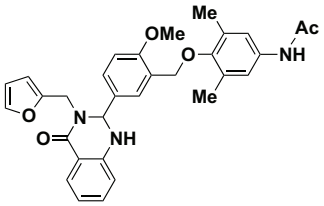
ML186
GPR55 antagonist
(*Heynen-Genel et al. 2010a)*



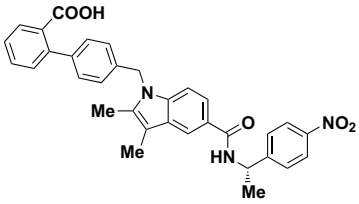
ML193
GPR55 agonist
(*Kotsikorou et al. 2013)*



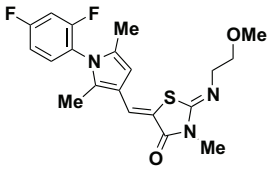
ML221
Apelin J receptor antagonist
(*Maloney et al. 2012)*



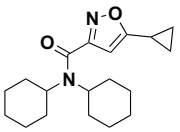
ML224
TSHR inverse agonist
(*Neumann et al. 2014)*



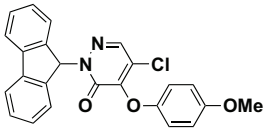
ML244
Inhibitor of Cdk5- mediated PPARγ phosphorylation
(*Choi et al., 2011; Kamenecka et al., 2010)*



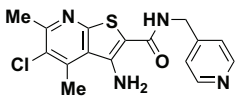
ML248
S1PR4 agonist
(*Guerrero et al., 2010b; Guerrero et al., 2012)*



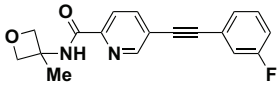
ML249
S1PR3 agonist
(*Guerrero et al., 2010a; Jo et al., 2012; Urbano et al., 2013)*



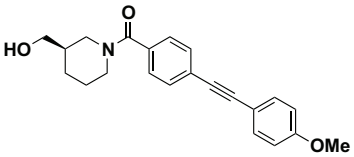
ML250
GPR7 antagonist
(*Guerrero et al. 2013)*



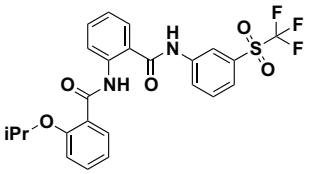
ML253
M4 AChR positive allosteric modulator
(*Le et al., 2013; Niswender et al., 2010)*



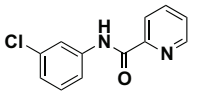
ML254
mGluR5 positive allosteric modulator
(*Zhou et al. 2010)*



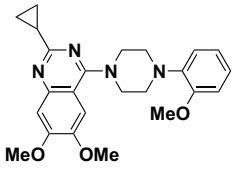
ML289
mGluR3 negative allosteric modulator
(*Sheffler et al. 2010)*



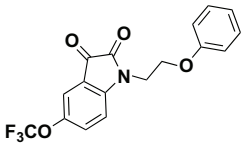
ML290
RXFP1 agonist
(*Xiao et al. 2013)*



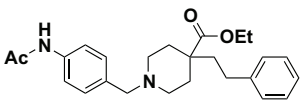
ML292
mGluR4 positive allosteric modulator
(*Engers et al. 2010)*



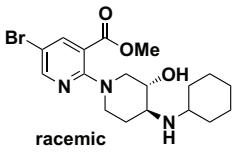
ML314
NTR1 β-arrestin biased agonist
(*Peddibhotla et al. 2013)*



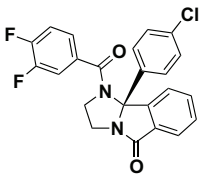
ML326
M5 AChR positive allosteric modulator
(*Gentry et al., 2010; Gentry et al., 2013)*



ML335
Inhibitor of OPRM1-OPRD1 heterodimerization
(*Gomes et al. 2013)*

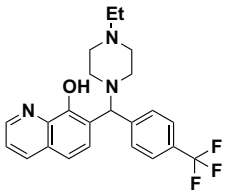


ML350
OPRK antagonist
(*Guerrero et al. 2010)*

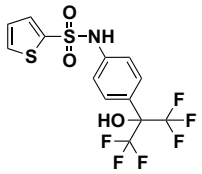


ML375
M5 AChR negative allosteric modulator
(*Gentry et al. 2013)*

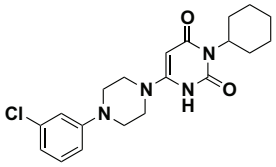
Receptor



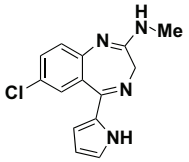
ML311
MCL1-BIM inhibitor
(*Bannister et al. 2010a)*



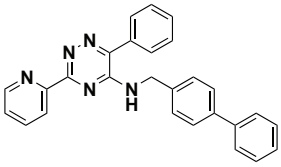
ML176
RORα inverse agonist
(*Kumar et al. 2011)*



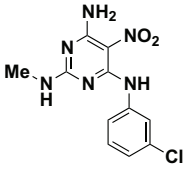
ML180
LRH1 inverse agonist
(*Busby et al. 2010)*



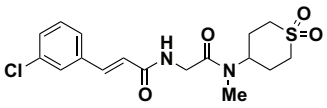
ML223
CBFβ-RUNX1 inhibitor
(*Cunningham et al. 2012)*



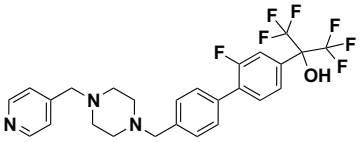
ML228
HIF activator
(*Theriault et al. 2010)*



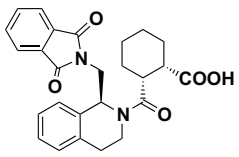
ML231
RTG branch of yeast TORC1 inhibitor
(*Chen et al. 2010)*



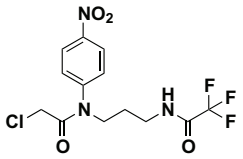
ML264
KLF5 inhibitor
(*Bialkowska et al. 2010)*



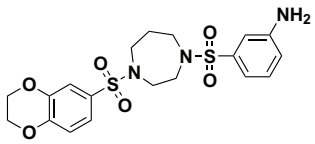
ML310
RORγ inverse agonist
(*Busby et al. 2010)*



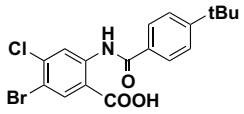
ML334
Non-covalent Keap1-Nrf2 inhibitor
(*Amundsen et al. 2012, PDB: 4l7b)*



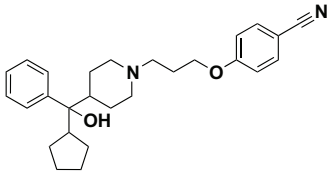
ML175
GSTO1 inhibitor
(*Tsuboi et al. 2011)*



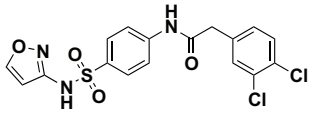
ML203
PKM2 activator
(*Boxer et al., 2010, PDB: 3me3)*



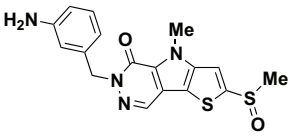
ML205
T. brucei HK1 inhibitor
(*Sharlow et al. 2010)*



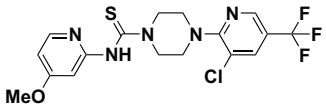
ML227
Menin-MLL inhibitor
(*Manka et al. 2010)*



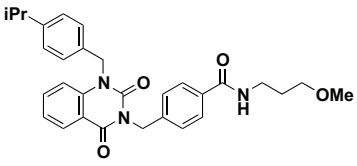
ML251
T. brucei phospho-fructokinase inhibitor
(*Walsh et al. 2010)*



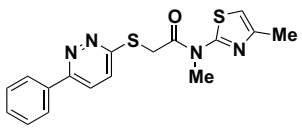
ML265
PKM2 activator
(*Boxer et al., 2010, PDB: 3u2z)*



ML267
Sfp-PPTase inhibitor
(*Foley et al. 2014)*

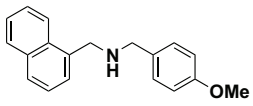


ML275
RSV polymerase inhibitor
(*Noah et al. 2010)*

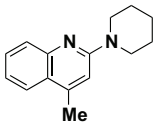


ML077
KCC2 antagonist
(*Lindsley et al. 2010)*

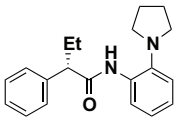
Signalling molecule Transcription factor Transferase Transporter



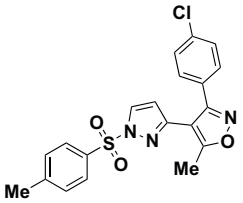
ML133
KCNJ2 inhibitor
(*Wang et al. 2011*)



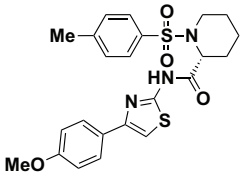
ML204
TRPC4 inhibitor
(*Miller et al. 2011*)



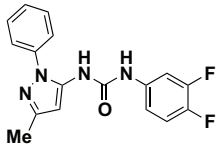
ML252
KCNQ2 inhibitor
(*Cheung et al. 2012*)



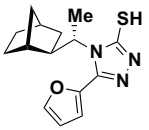
ML269
TRPML3 agonist
(*Grimm et al. 2010*)



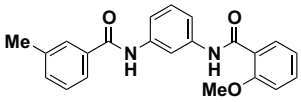
ML277
KCNQ1 activator
(*Mattmann et al. 2012, Yu et al. 2013*)



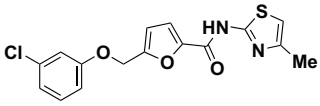
ML297
GIRK activator
(*Days et al. 2010*)



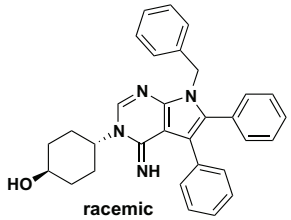
ML308
KCNK9 inhibitor
(*Miller et al. 2010*)



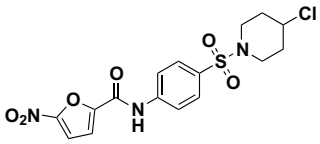
ML365
KCNK3 inhibitor
(*Zou et al. 2010*)



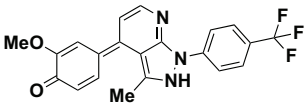
ML245
Breast cancer stem cell inhibitor
(*Carmody et al. 2010*)



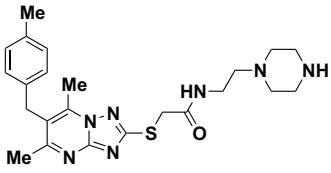
ML246
Inhibitor of PNC prevelance
(*Norton et al. 2009*)



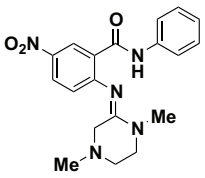
ML291
CHOP pathway agonist that activates the UPR
(*Flaherty et al. 2010*)



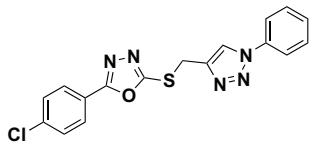
ML303
Influenza virus NS1 antagonist
(*Patnaik et al. 2010*)



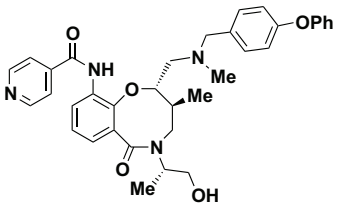
ML322
Inhibitor of HCV core dimerization
(*Kota et al. 2010*)



ML336
Inhibitor of VEEV replication protein
(*Chung et al. 2010*)



ML338
Non-replicating Mtb inhibitor
(*Nag et al. 2010*)



ML341
T. cruzi antimicrobial
(*Carmody et al., 2010; Dandapani et al., 2014*)

■ Transporter

Supplementary Table 1. Noteworthy MLP probes. The MLP Network identified numerous small-molecule probes, a subset of which are highlighted here, that act against a target for which a reasonably selective small-molecule was previously unavailable or that modulate a target via a novel mechanism of action. In analogy to language often used in the pharmaceutical industry to describe the initial member of a new drug class, these small molecules can be considered 'first-in-class' probes. Some of these initial probes may lack optimal potency or selectivity or may contain reactive functional groups that would ideally be excluded from probe compounds. However even when these limitations apply, these probes are a particularly critical advance because each provides a new tool for investigating emerging biology and alters the perception of what is 'druggable'.

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