SUPPLEMENTARY MATERIAL

The Influence of Target Family and Functional Activity on the Physicochemical Properties of Pre-Clinical Compounds.

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Tables of differences in the median property values and related p values for the target families.
Table of Pearson correlation coefficients for the 6 physicochemical properties.
Definition of Hydrogen Bond Donors and Acceptor and Rotatable bonds.

Table 1 Mann-Whitney point estimates for the differences in the MW population medians between the subsets and p values.

	esterases	**GPCRs (all)**	**GPCRs (monoamine)**	**GPCRs (peptide)**	**integrin receptor**	**ion channels**	**kinases**	**nuclear receptors**	**oxidases**	**PDEs**	**proteases**	**transporte**
GPCRs (all)	42.11 **0.0438**											
GPCRs (monoamine)	-15.91 0.3741											
GPCRs (peptide)	117.05 **0.0000**		134.12 **0.0000**									
integrin receptor	88.88 **0.0000**	51.01 **0.0048**	109.44 **0.0000**	-23.45 0.1871								
ion channels	-23.33 0.2173	-65.91 **0.0000**	-5.38 0.6017	-140.08 **0.0000**	-116.09 **0.0000**							
kinases	8.97 0.5553	-32.17 **0.0022**	28.03 **0.0086**	-105.68 **0.0000**	-82.11 **0.0000**	33.14 **0.0058**						
nuclear receptors	39.05 **0.0255**	-4.37 0.6551	55.17 **0.0000**	-78.06 **0.0000**	-52.72 **0.0010**	61.74 **0.0000**	28.11 **0.0083**					
oxidases	-33.98 **0.0706**	-80.04 **0.0000**	-18.96 0.1425	-152.74 **0.0000**	-124.98 **0.0000**	-12.05 0.3718	-45.85 **0.0010**	-73.34 **0.0000**				
PDEs	70.73 **0.0037**	29.9 0.1135	90.42 **0.0000**	-44.21 **0.0135**	-21 0.3487	94.93 **0.0000**	62.75 **0.0006**	33.57 **0.0476**	109.05 **0.0000**			
proteases	77.94 **0.0002**	30.12 **0.0005**	91.11 **0.0000**	-42.91 **0.0000**	-16.47 0.3418	98.14 **0.0000**	65.72 **0.0000**	36.88 **0.0004**	112.04 **0.0000**	0.09 0.9824		
transporters	-57.53 **0.0054**	-101.4 **0.0000**	-40.15 **0.0022**	-174.85 **0.0000**	-152.13 **0.0000**	-35.44 **0.0139**	-69.24 **0.0000**	-97.62 **0.0000**	-21.94 0.1529	-132.06 **0.0000**	-133.11 **0.0000**	
transferases	126.4 **0.0005**	90.26 **0.0000**	149.08 **0.0000**	14.99 0.5018	30.8 0.3083	155.75 **0.0000**	118.13 **0.0000**	91.71 **0.0001**	168.1 **0.0000**	64.07 **0.0696**	58.66 **0.0126**	188.6 **0.0000**

Bold text indicates significance at the 90% level ($p < 0.1$)

Table 2 Mann-Whitney point estimates for the differences in the cLogP population medians between the subsets and p values.

	esterases	**GPCRs (all)**	**GPCRs (monoamine)**	**GPCRs (peptide)**	**integrin receptor**	**ion channels**	**kinases**	**nuclear receptors**	**oxidases**	**PDEs**	**proteases**	**transporter**
GPCRs (all)	0.1 0.7000											
GPCRs (monoamine)	-0.5 0.1000											
GPCRs (peptide)	0.8 **0.0443**		1.2 **0.0000**									
integrin receptor	-1.5 **0.0109**	-1.6 **0.0000**	-1.0 **0.0088**	-2.2 **0.0000**								
ion channels	-1.2 **0.0178**	-1.3 **0.0000**	-0.7 **0.0010**	-1.9 **0.0000**	0.3 0.5549							
kinases	-0.6 0.1004	-0.8 **0.0000**	-0.2 0.4000	-1.4 **0.0000**	0.8 **0.0670**	0.5 0.1000						
nuclear receptors	1.0 **0.0209**	0.9 **0.0000**	1.5 **0.0000**	0.2 0.2000	2.6 **0.0000**	2.2 **0.0000**	1.7 **0.0000**					
oxidases	-0.1 0.8419	-0.2 0.5000	0.4 0.1000	-0.8 **0.0021**	1.7 **0.0000**	1.1 **0.0023**	0.6 0.1000	-1.0 **0.0004**				
PDEs	-0.7 **0.0470**	-0.8 **0.0020**	-0.2 0.4000	-1.4 **0.0000**	1.5 **0.0054**	0.5 0.1340	0.0 0.8836	-1.6 **0.0000**	-0.6 0.1000			
proteases	-1.2 **0.0010**	-1.3 **0.0000**	-0.7 **0.0000**	-2.0 **0.0000**	0.5 0.2500	0.0 0.9000	-0.5 **0.0000**	-2.2 **0.0000**	-1.1 **0.0000**	-0.5 **0.0000**		
transporters	-0.4 0.3791	-0.4 **0.0395**	0.2 0.4000	-1.0 **0.0000**	1.3 **0.0077**	0.9 **0.0029**	0.4 0.1933	-1.3 **0.0000**	-0.3 0.5000	0.3 0.2310	0.9 **0.0000**	
transferases	0.2 0.7319	-0.1 0.8000	0.6 **0.0000**	-0.7 **0.0089**	1.5 **0.0022**	1.3 **0.0010**	0.7 **0.0109**	-0.9 **0.0041**	0.2 0.7350	0.8 **0.0270**	1.3 **0.0000**	0.4 0.2619

Bold text indicates significance at the 90% level ($p < 0.1$)

Table 3 Mann-Whitney point estimates for the differences in the PSA population medians between the subsets and p values.

	esterases	**GPCRs (all)**	**GPCRs (monoamine)**	**GPCRs (peptide)**	**integrin receptor**	**ion channels**	**kinases**	**nuclear receptors**	**oxidases**	**PDEs**	**proteases**	**transporter**
GPCRs (all)	-2.5 0.5692											
GPCRs (monoamine)	-13.3 **0.0025**											
GPCRs (peptide)	7.6 0.1131		21.3 **0.0000**									
integrin receptor	36.1 **0.0000**	38.9 **0.0000**	49.8 **0.0000**	28.2 **0.0000**								
ion channels	0.88 0.7861	3.65 0.1170	14.06 **0.0000**	-6.8 **0.0116**	-35.6 **0.0000**							
kinases	13.85 **0.0085**	16.0 **0.0000**	26.0 **0.0000**	5.33 **0.0560**	-23.5 **0.0000**	12.81 **0.0000**						
nuclear receptors	-3.52 0.4929	-0.36 0.8658	10.57 **0.0000**	-10.8 **0.0000**	-39.4 **0.0000**	-3.74 0.1739	-15.8 **0.0000**					
oxidases	-9.8 **0.0323**	-7.5 **0.0183**	3.3 0.2668	-18.1 **0.0000**	-46.5 **0.0000**	-10.6 **0.0021**	-22.7 **0.0000**	-7.3 **0.0413**				
PDEs	13.8 **0.0324**	15.6 **0.0002**	26.1 **0.0000**	5.07 0.2746	-23.4 **0.0000**	12.3 **0.0040**	0.46 0.9093	15.3 **0.0003**	22.9 **0.0000**			
proteases	33.5 **0.0000**	36.2 **0.0000**	47.2 **0.0000**	25.3 **0.0000**	-3.0 0.5567	32.6 **0.0000**	20.9 **0.0000**	36.5 **0.0000**	44.0 **0.0000**	21.4 **0.0000**		
transporters	-26.3 **0.0000**	-24.6 **0.0000**	-14.42 **0.0000**	-35.3 **0.0000**	-63.5 **0.0000**	-27.96 **0.0000**	-40.7 **0.0000**	-24.6 **0.0000**	-17.64 **0.0000**	-41.2 **0.0000**	-62.0 **0.0000**	
transferases	30.6 **0.0007**	32.6 **0.0000**	43.4 **0.0000**	23.02 **0.0000**	-6.28 0.4454	28.3 **0.0000**	14.7 **0.0077**	33.6 **0.0000**	40.8 **0.0000**	18.0 **0.0188**	-2.19 0.7093	56.6 **0.0000**

Bold text indicates significance at the 90% level ($p < 0.1$)

Table 4 Mann-Whitney point estimates for the differences in the HBA population medians between the subsets and p values.

	esterases	**GPCRs (all)**	**GPCRs (monoamine)**	**GPCRs (peptide)**	**integrin receptor**	**ion channels**	**kinases**	**nuclear receptors**	**oxidases**	**PDEs**	**proteases**	**transporter**
GPCRs (all)	0 0.7556											
GPCRs (monoamine)	-1.0 **0.0176**											
GPCRs (peptide)	1.0 0.1142		1.0 **0.0000**									
integrin receptor	2.0 **0.0000**	2.0 **0.0000**	3.0 **0.0000**	1.0 **0.0001**								
ion channels	0 0.9789	0 0.5640	1 **0.0000**	-1.0 **0.0012**	-2.0 **0.0000**							
kinases	0 0.2566	1.0 **0.0027**	1.0 **0.0000**	0 0.3347	-1.0 **0.0000**	0 **0.0268**						
nuclear receptors	0 0.2963	0 0.1106	0 **0.0323**	-1.0 **0.0000**	-2.0 **0.0000**	0 **0.0888**	-1.0 **0.0006**					
oxidases	-1.0 **0.0254**	-1.0 **0.0013**	0.0 0.6187	-1.0 **0.0000**	-3.0 **0.0000**	-1.0 **0.0010**	-1.0 **0.0000**	0.0 **0.0832**				
PDEs	1.0 **0.0243**	1.0 **0.0002**	2.0 **0.0000**	0 0.1677	-1.0 **0.0266**	1.0 **0.0006**	1 **0.0261**	1.0 **0.0001**	2.0 **0.0000**			
proteases	1.0 **0.0010**	1.0 **0.0000**	2.0 **0.0000**	1.0 **0.0001**	-1.0 **0.0556**	1.0 **0.0000**	1.0 **0.0000**	2.0 **0.0000**	2.0 **0.0000**	0.0 0.3393		
transporters	-1.0 **0.0001**	-1.0 **0.0000**	-1 **0.0003**	-2.0 **0.0000**	-3.0 **0.0000**	-1 **0.0000**	-2.0 **0.0000**	-1.0 **0.0000**	-1 **0.0291**	-2.0 **0.0000**	-3.0 **0.0000**	
transferases	1.0 **0.0057**	2.0 **0.0000**	2.0 **0.0000**	1 **0.0098**	0 0.3537	1.0 **0.0000**	1.0 **0.0028**	2.0 **0.0000**	2.0 **0.0000**	0.0 0.3472	0 0.5573	3.0 **0.0000**

Bold text indicates significance at the 90% level ($p < 0.1$)

Table 5 Mann-Whitney point estimates for the differences in the HBD population medians between the subsets and p values.

	esterases	**GPCRs (all)**	**GPCRs (monoamine)**	**GPCRs (peptide)**	**integrin receptor**	**ion channels**	**kinases**	**nuclear receptors**	**oxidases**	**PDEs**	**proteases**	**transporter**
GPCRs (all)	0 0.3											
GPCRs (monoamine)	0.0 **0.0457**											
GPCRs (peptide)	0.0 0.8491		0.0 **0.0000**									
integrin receptor	1.0 **0.0009**	2.0 **0.0000**	2.0 **0.0000**	1.0 **0.0000**								
ion channels	0.0 0.2784	1 **0.0000**	1 **0.0000**	0.0 **0.0222**	-1.0 **0.0008**							
kinases	1 **0.0009**	1.0 **0.0000**	1.0 **0.0000**	1 **0.0000**	0.0 0.2223	1 **0.0005**						
nuclear receptors	0.0 **0.0498**	0.0 0.1472	0.0 0.5803	0.0 **0.0020**	-2.0 **0.0000**	-1 **0.0000**	-1.0 **0.0000**					
oxidases	-1.0 **0.0133**	0.0 **0.0127**	0.0 0.2381	-1.0 **0.0004**	-2.0 **0.0000**	-1.0 **0.0000**	-1.0 **0.0000**	0.0 0.1374				
PDEs	0.0 0.2008	0.0 0.6940	0.0 0.4620	0.0 0.1443	-1.0 **0.0000**	-1.0 **0.0063**	-1 **0.0000**	0.0 0.6819	0.0 0.1404			
proteases	2.0 **0.0000**	2.0 **0.0000**	2.0 **0.0000**	2.0 **0.0000**	0.0 0.3593	1.0 **0.0013**	1.0 **0.0013**	2.0 **0.0000**	2.0 **0.0000**	2.0 **0.0000**		
transporters	-1.0 **0.0038**	0 **0.0012**	0 **0.0770**	-1.0 **0.0000**	-2.0 **0.0000**	-1 **0.0000**	-2.0 **0.0000**	0.0 **0.0274**	0.0 0.6915	0.0 **0.0501**	-2.0 **0.0000**	
transferases	1.0 **0.0057**	1.0 **0.0000**	1.0 **0.0000**	1 **0.0000**	0 0.7452	1.0 **0.0030**	0.0 0.4788	1.0 **0.0000**	2.0 **0.0000**	1.0 **0.0001**	0 0.2572	2.0 **0.0000**

Bold text indicates significance at the 90% level ($p < 0.1$)

Table 6 Mann-Whitney point estimates for the differences in the RB population medians between the subsets and p values.

	esterases	**GPCRs (all)**	**GPCRs (monoamine)**	**GPCRs (peptide)**	**integrin receptor**	**ion channels**	**kinases**	**nuclear receptors**	**oxidases**	**PDEs**	**proteases**	**transporter**
GPCRs (all)	0 0.9905											
GPCRs (monoamine)	-1.0 **0.0388**											
GPCRs (peptide)	1.0 **0.0324**		3.0 **0.0000**									
integrin receptor	3.0 0.0028	3.0 **0.0000**	4.0 **0.0000**	1.0 **0.0350**								
ion channels	-1 0.1143	-1 **0.0002**	0 0.8717	-3.0 **0.0000**	-4.0 **0.0000**							
kinases	-1 **0.0696**	-1.0 **0.0003**	0.0 0.5147	-2 **0.0000**	-4.0 **0.0000**	0 0.4875						
nuclear receptors	-2 **0.0632**	-2 **0.0000**	0 0.4362	-3.0 **0.0000**	-4.0 **0.0000**	-1 0.2534	-1.0 0.1249					
oxidases	-2.0 **0.0022**	-2.0 **0.0000**	-1.0 **0.0152**	-3.0 **0.0000**	-5.0 **0.0000**	-1.0 **0.0356**	-1.0 **0.0021**	0.0 0.4170				
PDEs	1.0 0.4941	1.0 0.3601	2.0 **0.0007**	-1 **0.0821**	-2.0 **0.0022**	2.0 **0.0059**	2 **0.0021**	2.0 **0.0054**	3.0 **0.0000**			
proteases	2.0 **0.0133**	2.0 **0.0000**	3.0 **0.0000**	0.0 0.4376	-1.0 **0.0699**	3.0 **0.0000**	3.0 **0.0000**	3.0 **0.0000**	4.0 **0.0000**	1.0 **0.0487**		
transporters	-2.0 **0.0133**	-2.0 **0.0000**	-1 **0.0645**	-3.0 **0.0000**	-5.0 **0.0000**	-1 **0.0534**	-1.0 **0.0135**	0.0 0.3985	0 0.9181	-2.0 **0.0002**	-4.0 **0.0000**	
transferases	4.0 **0.0001**	4.0 **0.0000**	5.0 **0.0000**	3 **0.0001**	1 0.3314	5.0 **0.0000**	5.0 **0.0000**	6.0 **0.0000**	6.0 **0.0000**	4.0 **0.0002**	2 **0.0006**	6.0 **0.0000**

Bold text indicates significance at the 90% level ($p < 0.1$)

Table 7 Pearson coefficients of correlation for the 6 physicochemical properties used in the analysis of the SCOPE target family ligands. In all cases, p = 0.000.

Property	MW	cLogP	PSA	HBA	HBD
cLogP	0.258				
PSA	0.734	-0.278			
HBA	0.755	-0.201	0.920		
HBD	0.398	-0.332	0.739	0.483	
RB	0.830	0.179	0.716	0.744	0.449

Definition of Hydrogen Bond Donors and Acceptor

The perception of hydrogen bond donors and acceptors is performed in two steps:

1. A simple default rule is applied to determine the donors and acceptors.
2. Then, a list of exceptions to the default rules is applied.

Default Rule

- Any nitrogen or oxygen atom with at least one pair of free electrons is considered as an acceptor.
- Any hydrogen atom that is bonded to a nitrogen or oxygen atom is considered as a donor.

Exceptions

- The nitrogen atoms of amides, sulfonamides, and equivalent structures are not considered as acceptors.
- Only one nitrogen atom of guanidines, amidines, and equivalent groups is considered as an acceptor.
- The nitrogen atoms of aromatic amines are not considered as acceptors.
- The nitrogen atoms of five-membered aromatic rings like pyrrole are not considered as acceptors.
- The sulfur atoms of thiocarbonyl compounds are considered as acceptors.

Definition of Rotatable Bonds

A bond is considered as being rotatable, if:

- it is not in a ring, or if it is in a ring larger than 8;
- it is a single or a triple bond;
- none of the two atoms is terminal;
- it is not adjacent to a triple bond;
- it is not an amide, amidine, guanidine bond.