CDK Profiler

REACTION BIOLOGY

TARGET-SPECIFIC ASSAY SERVICES

The CDK Profiler is performed with ^{33}PanQinase™ assay technology at our German site.

The Service in Brief

The CDK Profiler service comprises biochemical activity testing of compounds against a panel of 43 CDK/Cyclin complexes formed from 20 CDKs and 16 cyclins. Each project includes testing one reference inhibitor from a selection of eight known CDK inhibitors.

Panel of available CDK/Cyclins

No. of complexes:	43 covering all 20 CDKs (table 1)
Species:	Human
Assay technology:	^{33}PanQinase™ activity assay. IC50 values with 10 concentrations.
Positive control:	One known CDK inhibitor can be selected as a reference compound (table 2)
Results type:	Report including IC50 values against 32 CDK/Cyclin complexes (table 3)

CDK1/CycA1	CDK6/CycD1
CDK1/CycA2	CDK6/CycD2
CDK1/CycB1	CDK6/CycD3
CDK1/CycE1	CDK7/CycH/MAT1
CDK1/CycE2	CDK8/CycC
CDK1/CycO	CDK9/CycK
CDK2/CycA1	CDK9/CycT1
CDK2/CycA2	CDK9/CycT2
CDK2/CycD1	CDK10/CycQ
CDK2/CycE1	CDK11B/CycK
CDK2/CycE2	CDK12/CycK
CDK2/CycO	CDK13/CycK
CDK3/CycC	CDK14/CycY
CDK3/CycE1	CDK15/CycA2
CDK3/CycE2	CDK15/CycB1
CDK3/CycO	CDK16/CycY
CDK4/CycD1	CDK17/CycY
CDK4/CycD2	CDK17/p35NCK
CDK4/CycD3	CDK18/CycY
CDK5/p25NCK	CDK19/CycC
CDK5/p35NCK	CDK20/CycH
	CDK20/CycT1

Table 1: *Panel of available CDK/Cyclins*

Name	Synonyms	Primary CDK-Target(s)
Abemaciclib	LY2835219	CDK4/6
Alvocidib	Flavopyridole	CDK9
CCT251545	HY-12681	CDK8
Dinaciclib	SCH727625	CDK1/5
Palbociclib	PD0332991	CDK4/6
Ponatinib	AP24534	CDK8/19
Ribociclib	LEE011	CDK4/6
Seliciclib	Roscovitine, CYC202	CDK2/5/9

Table 2: *Reference CDK inhibitors*

CDK/Cyclin Reference Compounds

Every CDK Profiler project includes one reference inhibitor with known activity against different members of the CDK/Cyclin kinase family. Customers can select a reference inhibitor according to their preferences from the eight clinical-stage or approved inhibitors (see table 2).

Example of application

Figure 1 shows a comparison of the profiles of two CDK4/CDK6 inhibitors, Palbociclib (yellow) and Abemaciclib (blue). In addition to differences in the potency against various CDKs, both inhibitors display different potencies against CDK6/type D cyclin complexes.

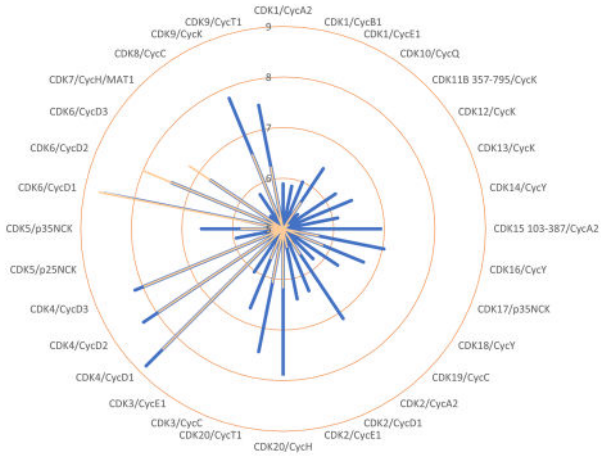

Figure 1: *CDK/Cyclin profiles (pIC50) of Palbociclib (yellow) and Abemaciclib (blue)*

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TARGET-SPECIFIC ASSAY SERVICES

IC_{50} >10^{-5} M | IC_{50} 10^{-7}-10^{-8} M | IC_{50} 10^{-6} -10^{-7} M | IC_{50} <10^{-8} M | IC_{50} <10^{-9} M

Compound	CDK1/CycA2	CDK1/CycB1	CDK1/CycE1	CDK2/CycA2	CDK2/CycD1	CDK2/CycE1	CDK3/CycC	CDK3/CycE1
	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)
Seliciclib (Roscovitine)	4.24E-06	5.23E-06	2.44E-06	7.66E-07	2.53E-06	2.67E-07	5.71E-06	1.06E-06
OTS964	>1E-05	>1E-05	>1E-05	3.97E-06	>1E-05	2.88E-06	>1E-05	>1E-05
NVP-2	1.72E-06	1.42E-06	8.46E-07	2.64E-06	5.82E-06	2.53E-06	2.04E-06	3.17E-06
Alvocidib (Flavopiridol)	6.02E-08	9.90E-08	2.03E-07	1.02E-07	3.15E-07	1.68E-07	2.04E-07	3.13E-07
Dinaciclib	7.85E-08	1.06E-07	3.55E-08	2.03E-08	4.40E-08	9.44E-09	5.23E-08	8.44E-09
Abemaciclib	1.30E-06	1.38E-06	9.98E-07	7.30E-08	4.70E-07	3.85E-07	2.02E-07	9.40E-07
CCT251545 (HY-12681)	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05
Ponatinib	>1E-05	>1E-05	7.52E-07	>1E-05	5.58E-07	>1E-05	5.57E-07	>1E-05
Ribociclib	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05
MC116.4	>1E-05	>1E-05	2.13E-07	>1E-05	1.09E-07	7.85E-06	1.36E-07	>1E-05
THZ531	>1E-05	>1E-05	5.74E-06	3.70E-06	6.67E-06	1.96E-06	4.24E-06	5.43E-06
Palbociclib	>1E-05	>1E-05	>1E-05	2.54E-06	9.38E-06	4.32E-06	2.32E-06	>1E-05

Compound	CDK4/CycD1	CDK4/CycD2	CDK4/CycD3	CDK5/p25NCK	CDK5/p35NCK	CDK6/CycD1	CDK6/CycD2	CDK6/CycD3
	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)
Seliciclib (Roscovitine)	>1E-05	>1E-05	>1E-05	1.47E-06	4.51E-07	>1E-05	>1E-05	>1E-05
OTS964	5.36E-06	7.55E-06	>1E-05	8.55E-06	2.98E-06	>1E-05	>1E-05	>1E-05
NVP-2	1.21E-06	3.57E-06	8.79E-06	3.93E-06	1.36E-06	2.32E-06	>1E-05	>1E-05
Alvocidib (Flavopiridol)	2.32E-08	2.59E-08	7.41E-08	2.92E-07	8.67E-08	4.41E-08	7.91E-07	2.39E-06
Dinaciclib	4.96E-08	4.40E-08	8.45E-08	2.09E-08	4.21E-09	1.75E-08	5.09E-07	1.25E-06
Abemaciclib	1.48E-09	4.81E-09	6.80E-09	1.13E-06	2.42E-07	2.64E-09	4.12E-08	1.86E-07
CCT251545 (HY-12681)	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05
Ponatinib	4.64E-06	8.40E-06	9.45E-06	>1E-05	>1E-05	5.91E-06	1.90E-06	8.69E-06
Ribociclib	8.94E-09	3.68E-08	3.43E-08	>1E-05	>1E-05	1.41E-08	1.09E-07	8.39E-07
MC116.4	3.61E-07	1.38E-06	1.67E-06	>1E-05	>1E-05	3.73E-06	1.21E-06	1.68E-06
THZ531	>1E-05	>1E-05	>1E-05	6.99E-06	2.78E-06	>1E-05	>1E-05	>1E-05
Palbociclib	4.41E-09	1.11E-08	1.08E-08	4.91E-06	1.48E-06	1.99E-09	1.00E-08	5.93E-08

Compound	CDK7/CycH/MAT1	CDK8/CycC	CDK9/CycK	CDK9/CycT1	CDK10/CycQ	CDK11B/CycK	CDK12/CycK	CDK13/CycK
	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)
Seliciclib (Roscovitine)	1.84E-06	>1E-05	1.19E-06	1.10E-06	>1E-05	>1E-05	3.77E-06	2.26E-06
OTS964	>1E-05	>1E-05	1.13E-06	1.30E-06	1.37E-06	3.69E-08	9.05E-06	5.88E-06
NVP-2	>1E-05	>1E-05	2.50E-09	2.59E-09	5.27E-08	6.25E-06	5.57E-08	9.87E-08
Alvocidib (Flavopiridol)	1.13E-06	5.80E-08	5.41E-09	4.08E-09	8.27E-08	3.55E-06	1.55E-07	1.43E-07
Dinaciclib	1.79E-07	4.63E-06	4.40E-09	4.33E-09	4.16E-08	7.85E-06	9.09E-09	8.87E-09
Abemaciclib	4.46E-06	1.53E-06	1.61E-08	3.24E-08	3.71E-07	3.94E-06	5.71E-07	3.44E-07
CCT251545 (HY-12681)	>1E-05	3.81E-08	2.96E-06	3.76E-06	>1E-05	>1E-05	>1E-05	>1E-05
Ponatinib	>1E-05	4.83E-08	2.84E-06	2.59E-06	1.14E-07	1.35E-06	2.13E-06	1.74E-06
Ribociclib	>1E-05	>1E-05	7.50E-07	1.15E-06	>1E-05	>1E-05	>1E-05	>1E-05
MC116.4	>1E-05	3.08E-08	3.18E-06	3.10E-06	2.76E-07	6.82E-07	>1E-05	6.30E-07
THZ531	2.22E-06	>1E-05	1.17E-06	1.01E-06	>1E-05	>1E-05	1.86E-07	>1E-05
Palbociclib	>1E-05	>1E-05	2.63E-07	5.77E-07	2.43E-06	>1E-05	7.35E-06	8.69E-06

Compound	CDK14/CycY	CDK15/CycA2	CDK16/CycY	CDK17/p35NCK	CDK18/CycY	CDK19/CycC	CDK20/CycH	CDK20/CycT1
	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)	IC50 (M)
Seliciclib (Roscovitine)	6.94E-06	3.82E-06	3.21E-06	>1E-05	2.63E-06	>1E-05	6.50E-06	4.89E-06
OTS964	>1E-05	>1E-05	4.54E-06	8.90E-06	>1E-05	>1E-05	>1E-05	>1E-05
NVP-2	>1E-05	2.03E-06	3.12E-06	4.51E-06	6.73E-06	>1E-05	1.08E-06	2.12E-07
Alvocidib (Flavopiridol)	1.82E-07	1.96E-08	6.40E-08	2.63E-06	1.80E-07	5.44E-08	1.29E-06	8.06E-07
Dinaciclib	3.63E-08	4.36E-08	1.66E-07	1.30E-06	1.51E-07	3.24E-06	5.76E-06	2.06E-07
Abemaciclib	7.97E-07	1.22E-07	9.29E-08	1.91E-07	5.01E-07	1.45E-06	1.38E-08	3.33E-08
CCT251545 (HY-12681)	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	1.19E-07	>1E-05	>1E-05
Ponatinib	1.67E-06	>1E-05	>1E-05	3.27E-06	4.30E-06	5.35E-08	>1E-05	6.45E-06
Ribociclib	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	>1E-05	9.14E-06
MC116.4	2.43E-06	>1E-05	1.54E-06	2.61E-06	4.73E-07	6.26E-08	>1E-05	>1E-05
THZ531	1.38E-07	8.31E-06	8.79E-06	8.81E-06	9.01E-06	>1E-05	5.04E-06	2.95E-06
Palbociclib	>1E-05	>1E-05	1.97E-06	1.44E-06	>1E-05	>1E-05	7.10E-07	8.40E-07

Table 3: *IC50 values determined in vitro for 12 small molecule inhibitors using 32 different CDK-Cyclin complexes, performed with the ^{33}PanQinase™ radiometric activity assay*