

## Catalogue of validated GPCR Ligands

In the following table we list the available ligands, with information about their selectivity, the emission and excitation wavelengths, their affinity measured by a radioligand binding assay and the specific further assays in which they have been validated.

Receptor	Code	$\lambda_{exc}/\lambda_{em}$	Affinity <sup>1</sup>	Selectivity <sup>1</sup>	Validation
<b>Dopamine Receptors</b>					
D <sub>2</sub>	CELT-174	589/616	1.06 nM	<b>Selective</b> K <sub>i</sub> (D <sub>3</sub> )=136.5 nM K <sub>i</sub> (D <sub>4</sub> )=152.7 nM	Fluorescence Microscopy in transfected cells Flow cytometry
	CELT-426	560/571	89.3 nM	<b>Partially Selective</b> K <sub>i</sub> (D <sub>3</sub> )=194.8 nM K <sub>i</sub> (D <sub>4</sub> )=263 nM	Fluorescence polarization Flow cytometry
D <sub>3</sub>	CELT-429	589/616	75.4 nM	<b>Selective</b> % displ.1 $\mu$ M (D <sub>2</sub> )= 6% % displ.1 $\mu$ M (D <sub>4</sub> )= 3%	Fluorescence Microscopy in transfected cells (ongoing)
	CELT-419	560/571	65.6 nM	<b>Partially Selective</b> K <sub>i</sub> (D <sub>2</sub> )=151.4 nM	Fluorescence polarization
	CELT-240 (D <sub>2</sub> /D <sub>3</sub> )	589/616	D <sub>3</sub> = 2.14 nM D <sub>2</sub> = 2.34 nM	<b>Selective against D<sub>4</sub></b> % displ.1 $\mu$ M(D <sub>4</sub> )=1%	Flow cytometry
D <sub>2</sub> /D <sub>3</sub>	CELT-241 (D <sub>2</sub> /D <sub>3</sub> )	646/662	D <sub>3</sub> = 4.77 nM D <sub>2</sub> = 5.22 nM	<b>Selective against D<sub>4</sub></b> K <sub>i</sub> (D <sub>4</sub> )=302.55 nM	Fluorescence Microscopy in transfected cells (ongoing)
<b>Adenosine Receptors</b>					
PAN-ADO	CELT-298	646/662	A <sub>1</sub> = 20.9 nM A <sub>2A</sub> = 171 nM A <sub>2B</sub> = 44.7 nM A <sub>3</sub> = 95.2 nM	<b>Non Selective</b>	Fluorescence Microscopy in transfected cells
A <sub>1</sub>	CELT-448	560/571	26.2 nM	<b>Selective</b> % displ.1 $\mu$ M (A <sub>2A</sub> )= 11% % displ.1 $\mu$ M (A <sub>2B</sub> )= 22% % displ.1 $\mu$ M (A <sub>3</sub> )= 24%	Fluorescence polarization (ongoing) Fluorescence Microscopy in transfected cells (ongoing)
	CELT-372 (A <sub>1</sub> /A <sub>2B</sub> )	589/616	A <sub>1</sub> = 1.89 nM A <sub>2B</sub> = 24.75 nM	<b>Partially Selective</b> K <sub>i</sub> (A <sub>2A</sub> )=80.33 nM K <sub>i</sub> (A <sub>3</sub> )=967.8 nM	Fluorescence Microscopy in transfected cells

	<b>CELT-360</b>	646/662	8.6 nM	<b>Non Selective</b> K <sub>i</sub> (A <sub>2A</sub> )=98.38 nM K <sub>i</sub> (A <sub>2B</sub> )=72.24 nM K <sub>i</sub> (A <sub>3</sub> )=231.01 nM	Fluorescence Microscopy in transfected cells
Receptor	Code	$\lambda_{exc}/\lambda_{em}$	Affinity <sup>1</sup>	Selectivity <sup>1</sup>	Validation
A <sub>2A</sub>	<b>CELT-316</b>	589/616	116.1 nM	<b>Selective</b> % displ.1 $\mu$ M (A <sub>1</sub> )= 18% % displ.1 $\mu$ M (A <sub>2B</sub> )= 33% % displ.1 $\mu$ M (A <sub>3</sub> )= 31%	Fluorescence Microscopy in native cells
	<b>CELT-300</b>	646/662	8.35 nM	<b>Selective</b> % displ.1 $\mu$ M (A <sub>1</sub> )= 31% % displ.1 $\mu$ M (A <sub>2B</sub> )= 18% % displ.1 $\mu$ M (A <sub>3</sub> )= 38%	Fluorescence Microscopy in transfected cells (ongoing)
A <sub>2B</sub> /A <sub>3</sub>	<b>CELT-327</b>	589/616	A <sub>2B</sub> = 35.6 nM A <sub>3</sub> = 45.7 nM	<b>Selective</b> % displ.1 $\mu$ M (A <sub>1</sub> )=41% % displ.1 $\mu$ M (A <sub>2A</sub> )=1%	Fluorescence Microscopy in native cells
A <sub>3</sub>	<b>CELT-228</b>	560/571	52.7 nM	<b>Selective</b> % displ.1 $\mu$ M (A <sub>1</sub> )= 2% % displ.1 $\mu$ M (A <sub>2A</sub> )= 1% % displ.1 $\mu$ M (A <sub>2B</sub> )= 5%	Fluorescence Microscopy in native cells Fluorescence polarization
	<b>CELT-171</b>	589/616	6.13 nM	<b>Selective</b> % displ.1 $\mu$ M (A <sub>1</sub> )=2.1% % displ.1 $\mu$ M (A <sub>2B</sub> )= 1.9%	Fluorescence Microscopy in transfected and native cells
Serotonin Receptors					
5HT <sub>2A</sub> /5HT <sub>2C</sub>	<b>CELT-402</b>	589/616	5HT <sub>2A</sub> =29.7 nM 5HT <sub>2C</sub> = 14.6 nM	<b>Selective</b> K <sub>i</sub> (5HT <sub>2B</sub> )=222.9 nM	Fluorescence Microscopy in transfected cells (ongoing)
5HT <sub>2B</sub>	<b>CELT-211</b>	589/616	56.32 nM	<b>Selective</b> % displ.1 $\mu$ M (5HT <sub>2A</sub> )=0.94% % displ.1 $\mu$ M (5HT <sub>2C</sub> )= 1.75%	Fluorescence Microscopy in transfected cells
Cannabinoid Receptors					
PAN-CB	<b>CELT-335</b>	646/662	CB <sub>1</sub> = 44.8 nM CB <sub>2</sub> = 7.4 nM	<b>Non Selective</b>	HTRF in adherent cells <sup>3</sup> High Content screening Fluorescence Microscopy in transfected cells
CB <sub>2</sub>	<b>CELT-331</b>	646/662	75.9 nM	<b>Selective<sup>2</sup></b> % displ.1 $\mu$ M (CB <sub>1</sub> )=20%	High Content screening Fluorescence Microscopy in transfected cells
Muscarinic Receptors					
M <sub>1</sub>	<b>NIR-CELT 195</b>	743/782	57.77 nM	No data	Fluorescence Microscopy in transfected cells (ongoing)

Glucagon-like peptide-1 Receptors					
GLP1	<b>CELT-111 (LUXendin551)</b>	551/576	7.2	<b>Selective<sup>4</sup></b>	Widefield/confocal/2-photon microscopy in live and fixed mammalian cells and tissue, as well as anaesthetized mice <sup>4</sup>
GLP1	<b>CELT-112 (LUXendin645)</b>	645/664	7.5	<b>Selective<sup>5</sup></b>	Widefield/confocal/2-photon microscopy in live and fixed mammalian cells and tissue, as well as anaesthetized mice <sup>5</sup> TR-FRET <sup>6,7,8</sup>
GLP1	<b>CELT-113 (LUXendin762)</b>	762/784	7.0	<b>Selective<sup>4</sup></b>	Widefield/confocal/2-photon microscopy in live and fixed mammalian cells and tissue, as well as anaesthetized mice <sup>4</sup> . Non-invasive fluorescence preclinical imaging

<sup>1</sup> K<sub>i</sub> or % of displacement at 1 μM measured by radioligand binding assay. In the case of GLP1R ligands corresponds to pIC50

<sup>2</sup> Development of a CB<sub>1</sub> selective ligand is ongoing.

<sup>3</sup> Lu Raich et al. "Similarities and differences upon binding of naturally occurring Δ<sup>9</sup>-tetrahydrocannabinol-derivatives to cannabinoid CB<sub>1</sub> and CB<sub>2</sub> receptors" Pharmacol. Res., 2021,174,105970.

<sup>4</sup> J. Ast, A. N. Novak, T. Podewin, N. H. F. Fine, B. Jones, A. Tomas, R. Birke, K. Roßmann, B. Mathes, J. Eichhorst, M. Lehmann, A. K. Linnemann, D. J. Hodson, J. Broichhagen, 2021, DOI 10.33774/chemrxiv-2021-7rngq.

<sup>5</sup> J. Ast, A. Arvaniti, N. H. F. Fine, D. Nasteska, F. B. Ashford, Z. Stamatakis, Z. Koszegi, A. Bacon, B. J. Jones, M. A. Lucey, S. Sasaki, D. I. Brierley, B. Hastoy, A. Tomas, G. D'Agostino, F. Reimann, F. C. Lynn, C. A. Reissaus, A. K. Linnemann, E. D'Este, D. Calebiro, S. Trapp, K. Johnsson, T. Podewin, J. Broichhagen, D. J. Hodson, Nat Commun 2020, 11, 467.

<sup>6</sup> A. Marzook, S. Chen, P. Pickford, M. Lucey, Y. Wang, I. R. Corrêa Jr, J. Broichhagen, D. J. Hodson, V. Salem, G. A. Rutter, T. M. Tan, S. R. Bloom, A. Tomas, B. Jones, Biochemical Pharmacology 2021, 190, 114656.

<sup>7</sup> M. Lucey, T. Ashik, A. Marzook, Y. Wang, J. Goulding, A. Oishi, J. Broichhagen, D. J. Hodson, J. Minnion, Y. Elani, R. Jockers, S. J. Briddon, S. R. Bloom, A. Tomas, B. Jones, Mol Pharmacol 2021, DOI 10.1124/molpharm.121.000270.

<sup>8</sup> Z. Fang, S. Chen, P. Pickford, J. Broichhagen, D. J. Hodson, J. Ivan R. Corrêa, S. Kumar, F. Görlitz, C. Dunsby, P. M. W. French, G. A. Rutter, T. Tan, S. R. Bloom, A. Tomas, B. Jones, ACS Pharmacology & Translational Science 2020, DOI 10.1021/acspsci.0c00022.

In case you are interested by any of these ligands and they have not been validated yet for the kind of assay you want to test, please let us know: based on our experience we could advise you about which fluorophore works better for each assay, and eventually develop new versions -i.e. keeping the pharmacophore but changing the fluorophore- in a turnaround of 4-6 weeks.

## Contact Information

✓ Sonia Martinez: [sonia.martinez@celtarys.com](mailto:sonia.martinez@celtarys.com), +34 628 11 40 50