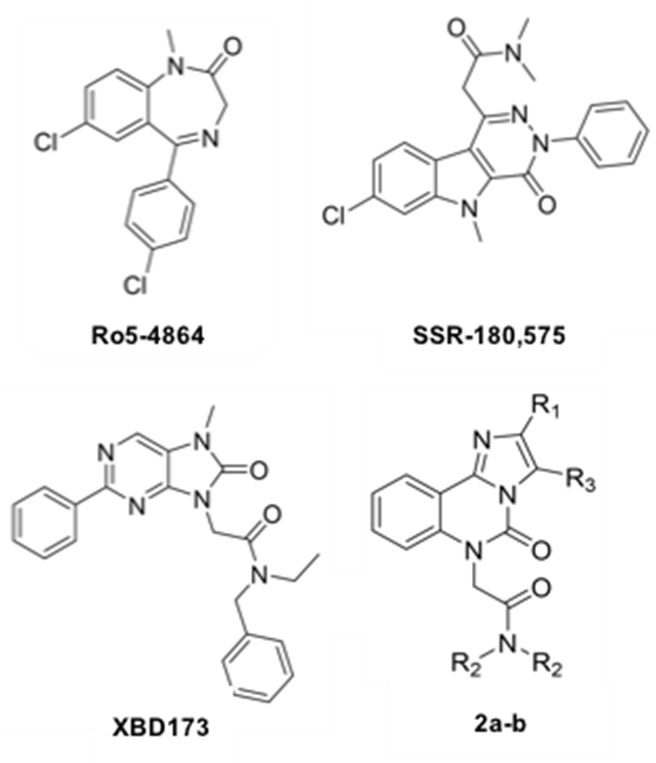
**Supplementary Material**

**TSPO Ligands Boost Mitochondrial Function and Pregnenolone Synthesis**



**Supplementary Figure 1.** TSPO ligands of references and the design of the imidazo[1,2-c]quinazolin-5-ones as new TSPO ligands. 2a is an 3-deaza analog derived from the CBR ligand CGS-13767. The insertion of an acetamide moiety as well as the transformation of the triazoloquinazoline scaffold into imidazoquinazoline led to compound 2a which showed no affinity for CBR up to 10 mM, but a promising affinity for TSPO with both [3H]-PK11195 and [3H]-Ro5-4864 (400 nM and 80 nM, respectively). 2a is a derivate of 2b and is structurally very close of it but with a drop of affinity (IC50 = 400 nM and 80 nM using [3H]-PK11195 and [3H]-Ro5-4864, respectively).



**Supplementary Figure 2.** aBinding assay performed on rat heart microsomes; bBinding assay performed on rat brain microsomes; cBinding assay performed on rat kidney mitochondrial fragments [1]; dBinding assay performed on rat brain with [3H]flunitrazepam [1]; end, not determined; fBinding assay performed on rat kidney membranes [2]; gBinding assay performed on rat cerebellum membranes [2];hBinding assay performed on rat whole brain mitochondrial fractions [3]; iBinding assay performed on rat cerebellum membranes [3].

**REFERENCES**

[1] Hirsch JD, Beyer CF, Malkowitz L, Loullis CC, Blume AJ (1989) Characterization of ligand binding to mitochondrial benzodiazepine receptors. *Mol Pharmacol* **35**, 164-172.

[2] Ferzaz B, Brault E, Bourliaud G, Robert JP, Poughon G, Claustre Y, Marguet F, Liere P, Schumacher M, Nowicki JP, Fournier J, Marabout B, Sevrin M, George P, Soubrie P, Benavides J, Scatton B (2002) SSR180575 (7-chloro-N,N,5-trimethyl-4-oxo-3-phenyl-3,5-dihydro-4H-pyridazino[4,5-b]indole-1-acetamide), a peripheral benzodiazepine receptor ligand, promotes neuronal survival and repair. *J Pharmacol Exp Ther* **301**, 1067-1078.

[3] Kita A, Kohayakawa H, Kinoshita T, Ochi Y, Nakamichi K, Kurumiya S, Furukawa K, Oka M (2004) Antianxiety and antidepressant-like effects of AC-5216, a novel mitochondrial benzodiazepine receptor ligand. *Br J Pharmacol* **142**, 1059-1072.