SUPPLEMENTARY INFORMATION

Rationally designed ruthenium complexes for breast cancer therapy

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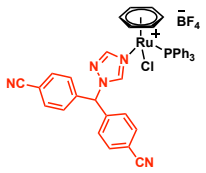
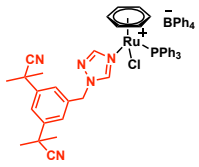
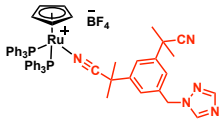
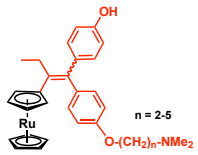
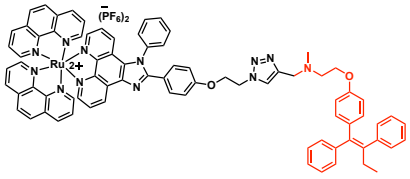
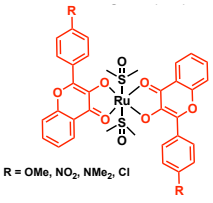
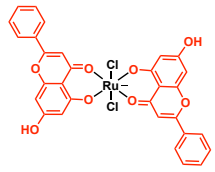
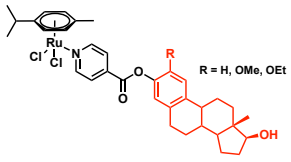
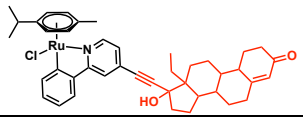
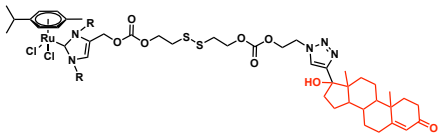
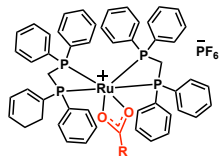
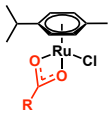
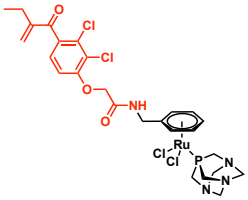
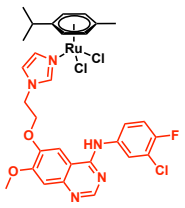
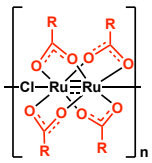
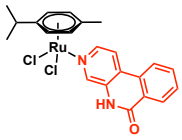
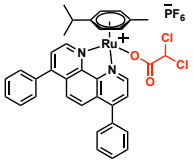
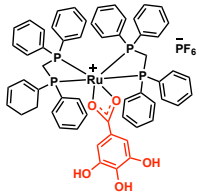
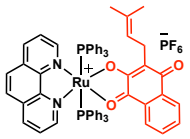
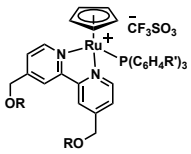
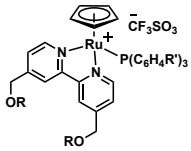
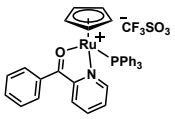
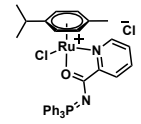
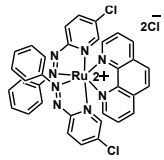
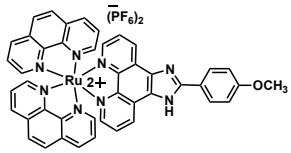
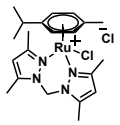
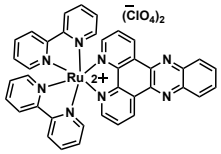
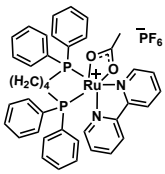
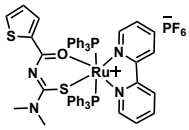
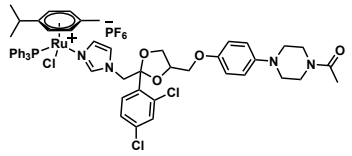
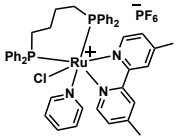
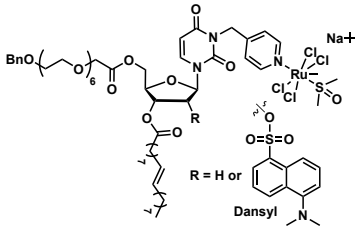
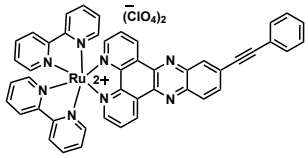
Table S1. Summary of the biological activity of the ruthenium complexes reviewed in this study.

		Bioactive ligand	In vitro IC_{50} (μM) values in breast cancer cells	In vivo antitumoral activity and/or in vivo toxicity
1		Aromatase inhibitor (letrozole)	>25 (MCF7)	N.A. [1]
2		Aromatase inhibitor (anastrozole)	≈ 4 (MCF7 and T47D)	No toxicity (12.5 μM) on the development of zebrafish embryos. [2]
3		Aromatase inhibitor (anastrozole)	0.50 ± 0.09 (MCF7) 0.32 ± 0.03 (T47D) 0.39 ± 0.09 (MDA-MB-231)	No toxicity (at concentrations around its IC_{50} values) on the development of zebrafish embryos. [3]
4		P450 enzyme inhibitor (etomidate)	N.A.	N.A. [4]
5		Steroid hormone receptor targeting molecules (tamoxifen derivatives)	>1 (MCF7)	N.A. [5]
6		Steroid hormone receptor targeting molecule (tamoxifen)	<8 (light) (MCF7) >16 (dark) (MCF7)	N.A. [6]
7		Steroid hormone receptor targeting molecule (flavone)	16.0 (MCF7) when R = OMe	N.A. [7]

8		Steroid hormone receptor targeting molecule (flavone)	> 100 (MCF7)	Mortality and body weight loss in rats (1000 mg/kg, at Day 20). [8]
9		Steroid hormone receptor targeting molecules (estradiol isonicotinates)	0.08 ± 0.04 (MCF7) when R = OEt	N.A. [9]
10		Steroid hormone receptor targeting molecule (levonorgestrel)	7.4 ± 0.1 (T47D)	N.A. [10]
11		Steroid hormone receptor targeting molecule (17α-ethynyl testosterone)	4.48 ± 0.17 (MCF7) 20.71 ± 0.92 (MDA-MB-231)	Slight decrease in tumor volume (2 μmol/kg, every 4 days, 5 doses) in mice bearing MCF7 cells. [11]
12		Nonsteroidal anti-inflammatory drugs (NSAIDs) (diclofenac, ibuprofen)	Ru-Dicl: 47 ± 6 (MCF7) Ru-Ibp: 9 ± 3 (MCF7)	N.A. [12]
13		Nonsteroidal anti-inflammatory drugs (NSAIDs) (diclofenac, ibuprofen, naproxen, aspirin)	<0.1 (MCF7) except when $RCOO^-$ = aspirin which was inactive	N.A. [13]
14		Glutathione S-transferase (GST) inhibitor (ethacrynic acid)	>20 (MCF7)	N.A. [14]
15		Epidermal growth factor (EGFR) inhibitors (4-anilinoquinazoline derivatives)	54 ± 4 (MCF7)	N.A. [15]

16		Nonsteroidal anti-inflammatory drugs (NSAIDs) (ibuprofen, naproxen)	Ru-Ibp-SPLNs: 70.3 ± 8.1 (MDA-MB-231) Ru-Npx-SPLNs: 101.8 ± 6.7 (MDA-MB-231)	N.A. [16]
17		Poly (ADP-ribose) polymerase (PARP) inhibitor	93.3 ± 11.4 (Hcc1937)	N.A. [17]
18		Aerobic glycolysis inhibitor (dichloroacetato)	0.86 ± 0.01 (MDA-MB-231)	N.A. [18]
19		Cell cycle arrest inducer (gallic acid)	0.81 ± 0.08 (MDA-MB-231) 1.0 ± 0.1 (MDA-MB-468)	N.A. [19]
20		Topoisomerase-interacting and ROS-generating molecule (lapachol)	0.20 ± 0.01 (MDA-MB-231)	N.A. [20]
21		Biotin	11.6 ± 1.5 (MDA-MB-231) 31.5 ± 4.7 (MCF7) when R = biotin and R′= H	Zebrafish tolerance up to 1.17 mg/L. Morphologic lesions such as curved spine/tail malformation, yolk sac and pericardial sac edema, cranial malformation and underdeveloped eyes were observed at 2.18 mg/L. [21]
22		Biotin	14.2 ± 0.7 when R′= F and R = biotin 7.7 ± 0.3 when R′= OCH_3 and R= biotin (MDA-MB-231) 22.4 ± 1.6 when R′= F and R= biotin 18.7 ± 1.6 R′= OCH_3 and R= biotin (MCF7)	LC_{50} values (lethality for 50% of the embryos/larvae) on zebrafish (120 hpf, 1.83-2.35 mg/L). Moderate to severe yolk sac edema and pericardial sac edema were observed. [22]

23		N.A.	0.03 ± 0.01 (MDA-MB-231)	Suppression of tumor growth (2.5 mg/kg/day, 10 days) in female athymic nude mice bearing MDA-MB-231 cells. No effect on the well-being of the animals. [23,24]
24		N.A.	2.61 ± 1.2 (MDA-MB-231)	Significant decrease (56%) in tumor volume (5 mg/kg, every other day, 14 doses) in NOD.CB17-Prkdc SCID/J mice bearing MDA-MB-23 cells. Low systemic toxicity. [25]
25		N.A.	1.8 ± 0.1 (HCC1937) 13.2 ± 0.3 (MDA-MB-231) 8.2 ± 0.1 (MCF7)	N.A. [26]
26		N.A.	14.6 ± 3.1 (MDA-MB-231) 78.0 ± 19.8 (MDA-MB-468) 28.0 ± 4.9 (MCF7)	N.A. [27]
27		N.A.	230.66 ± 0.02 (A17) 409.89 ± 0.04 (MDA-MB-231)	Suppression of tumor growth (52.5 mg/kg, every 3 days, 4 doses) in female FVB/NCrl mice bearing A17 cells. No apparent toxicity. [28]
28		N.A.	<4 (when complex is encapsulated)	Suppression of tumor growth (5 mg/kg/week, 4 doses) (encapsulated complex) in athymic nude mice bearing MDA-MB-231 cells. No apparent toxicity. [29]
29		N.A.	31.16 ± 0.04 (MDA-MB-231) >200 (MCF7)	N.A. [30]
30		N.A.	8.81 ± 0.81 (MDA-MB-231)	Low toxicity (up to 300 mg/kg, 14 days) in a Swiss mice model. [31]

31		N.A.	0.62 ± 0.02 (MDA-MB-231)	N.A. [32]
32		N.A.	9.18 ± 0.30 (MDA-MB-231)	N.A. [33]
33		N.A.	12.1 ± 3 (MDA-MB-231) 12.7 ± 4 (MCF7) (when R= H) Concentrations correspond to the effective metal concentration (15% mol/mol) carried by nanoaggregates	Suppression of tumor growth (15 mg/kg/week, 28 days) in athymic nude mice bearing MCF7 cells. No apparent toxicity. [34]
34		N.A.	17.2 ± 0.9 (MDA-MB-231) 74.9 ± 3.5 (MCF7)	Inhibition of cancer cell proliferation and metastasis (5 μM, 72 h) in a xenograft model of human MDA-MB-231 cells in zebrafish. [35]

References

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