Does CTR2 quaternary structure determine sensitivity of BCa cell lines to cisplatin?

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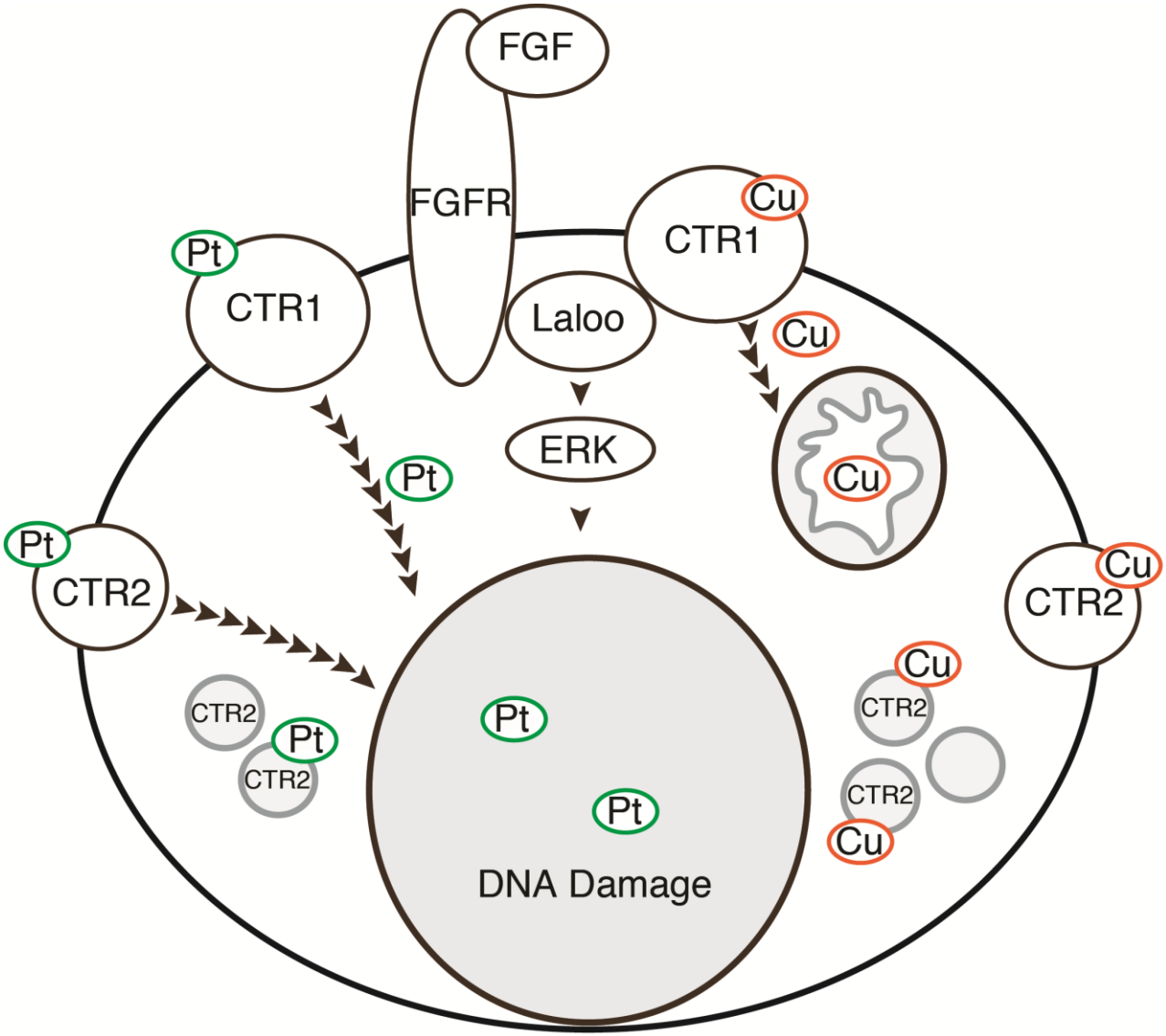
Discipline of Physiology, School of Medical Sciences and Bosch Institute, University of Sydney

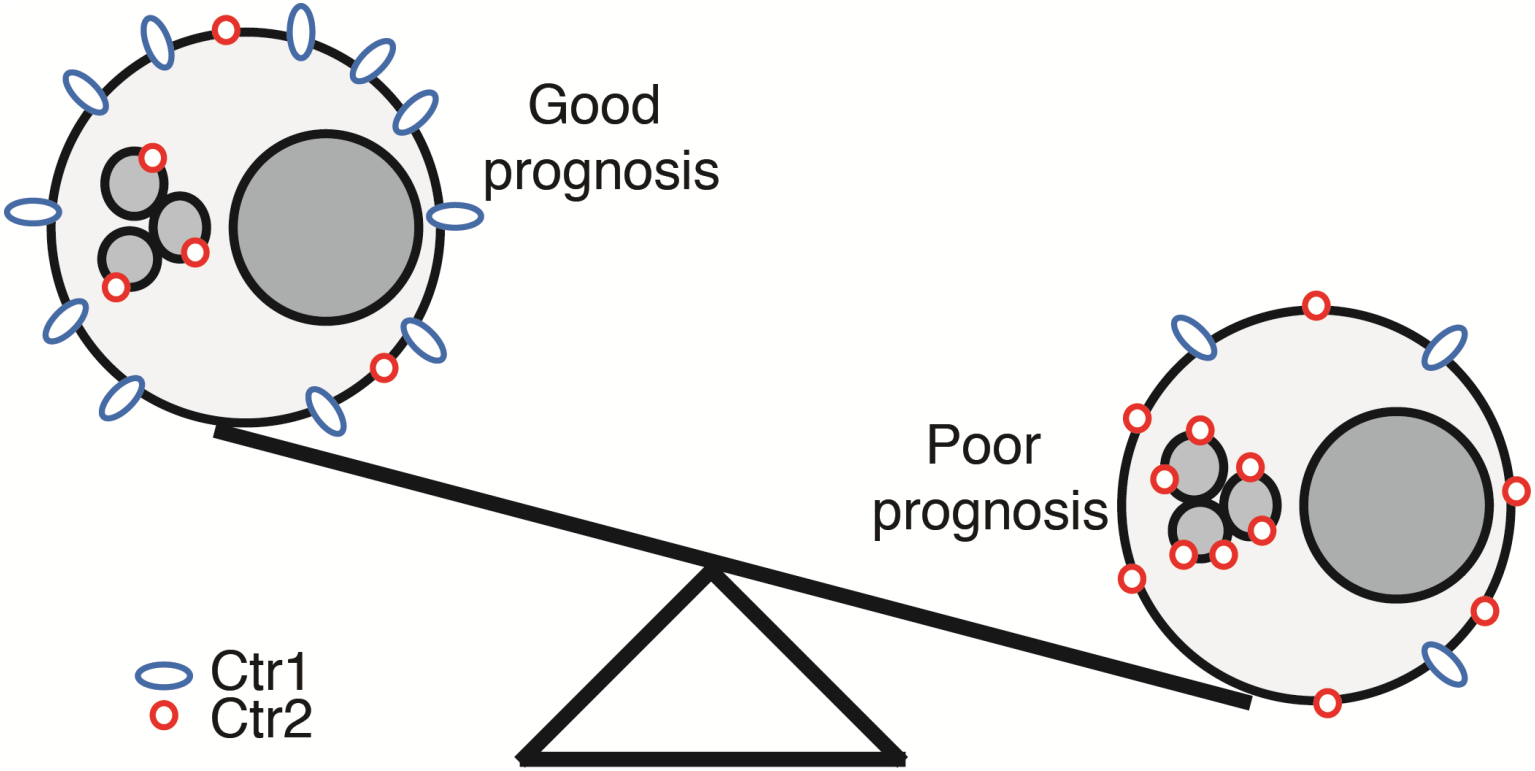
Cellular influx of reduced copper is mediated by CTR1 and 2



Levels of CTR1 and 2 have been related to sensitivity to platinum drugs

CTR1 associated with increased sensitivity and prognosis in lung and ovarian cancer (Chen *et al*., 2012)

Increased CTR2 associated with poor prognosis in breast and ovarian cancer (Ishida *et al*., 2010).

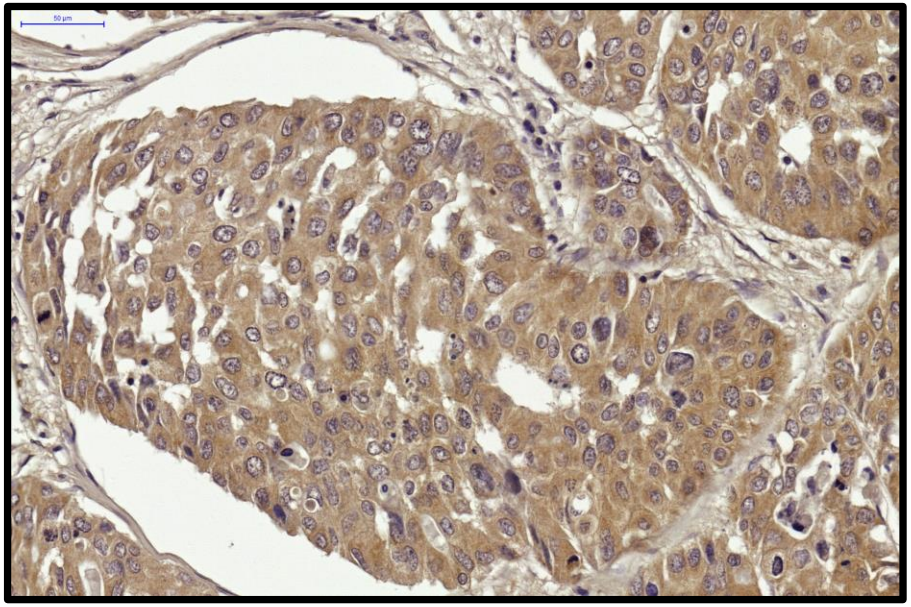


Wee, Weinstein, Fraser & Assinder (2013) Int J Biochem Cell Biol 45: 960-963.

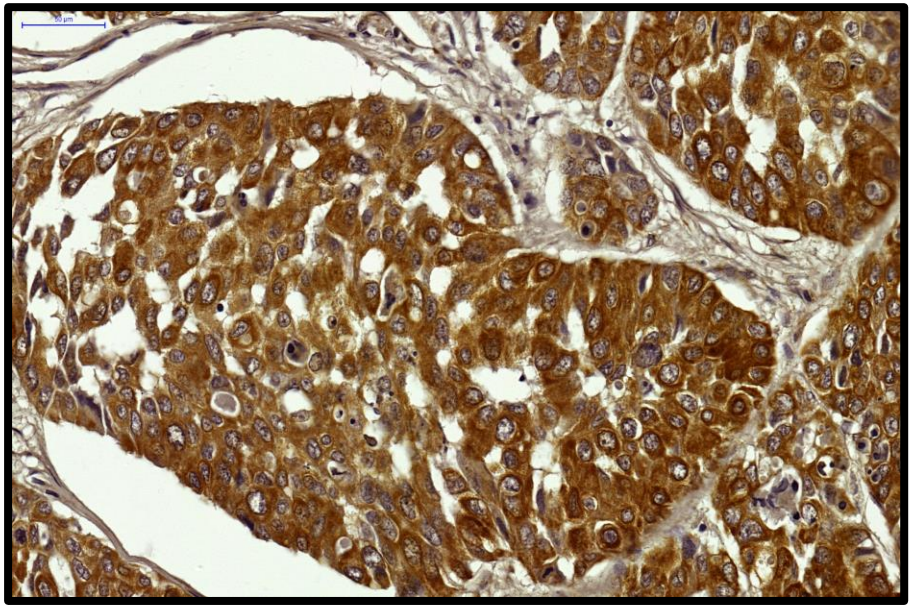
Hypothesis: Ductal and lobular breast carcinomas display greater CTR2:CTR1

Approach:
BCa TMAs (208 biopsy cores) analysed by immunocytochemistry, scored by blinded independent observer.

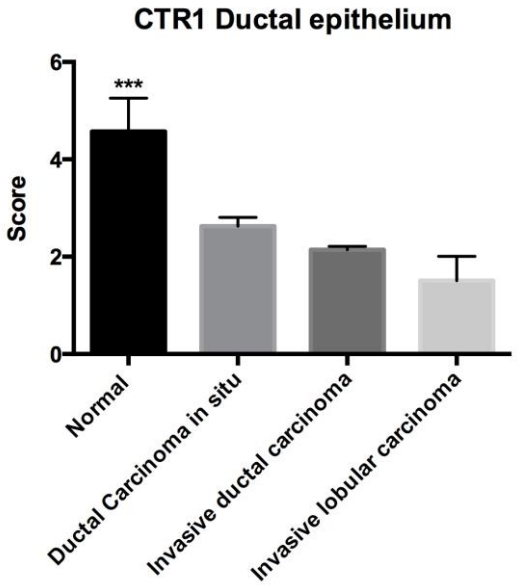
CTR1

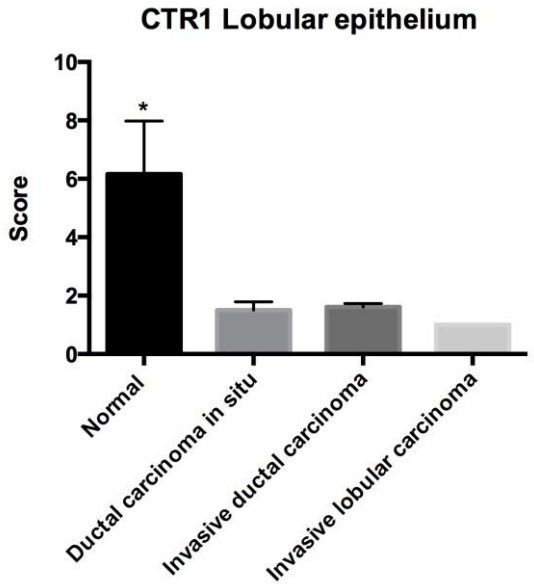


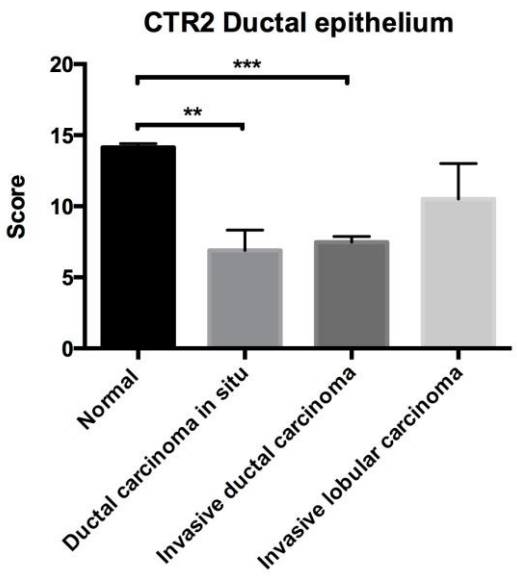
CTR2

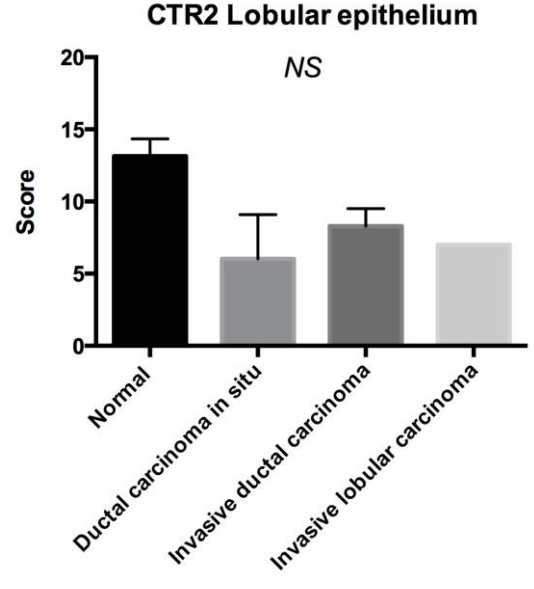


Both CTR1 and CTR2 are decreased in BCa

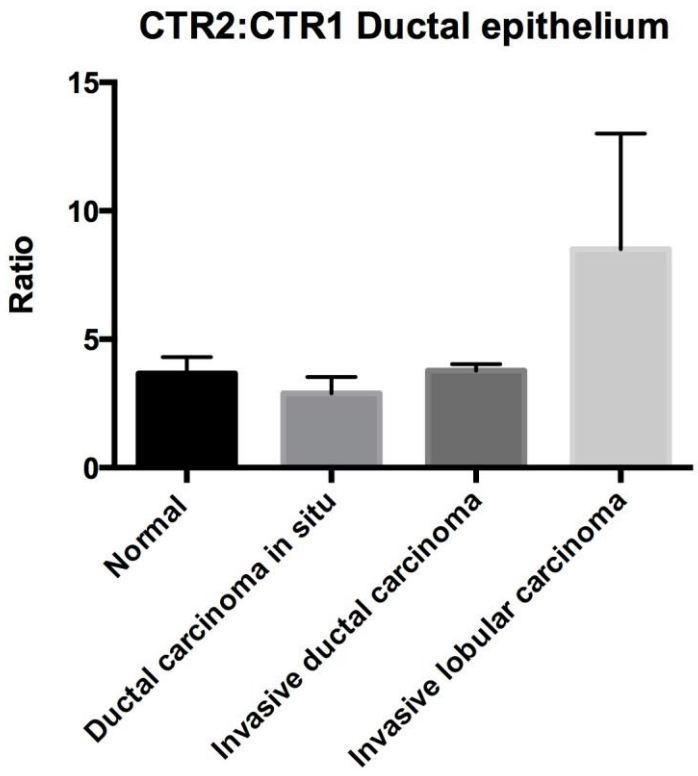


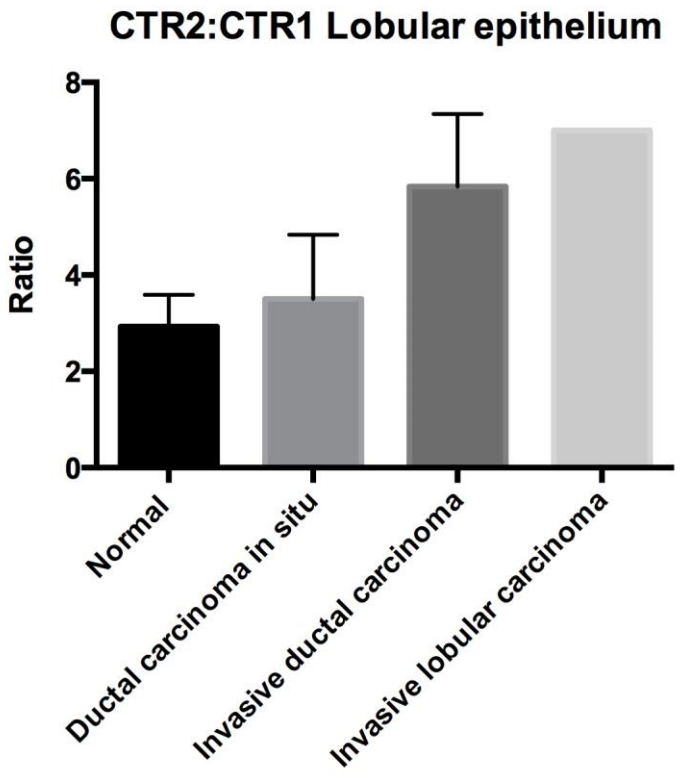




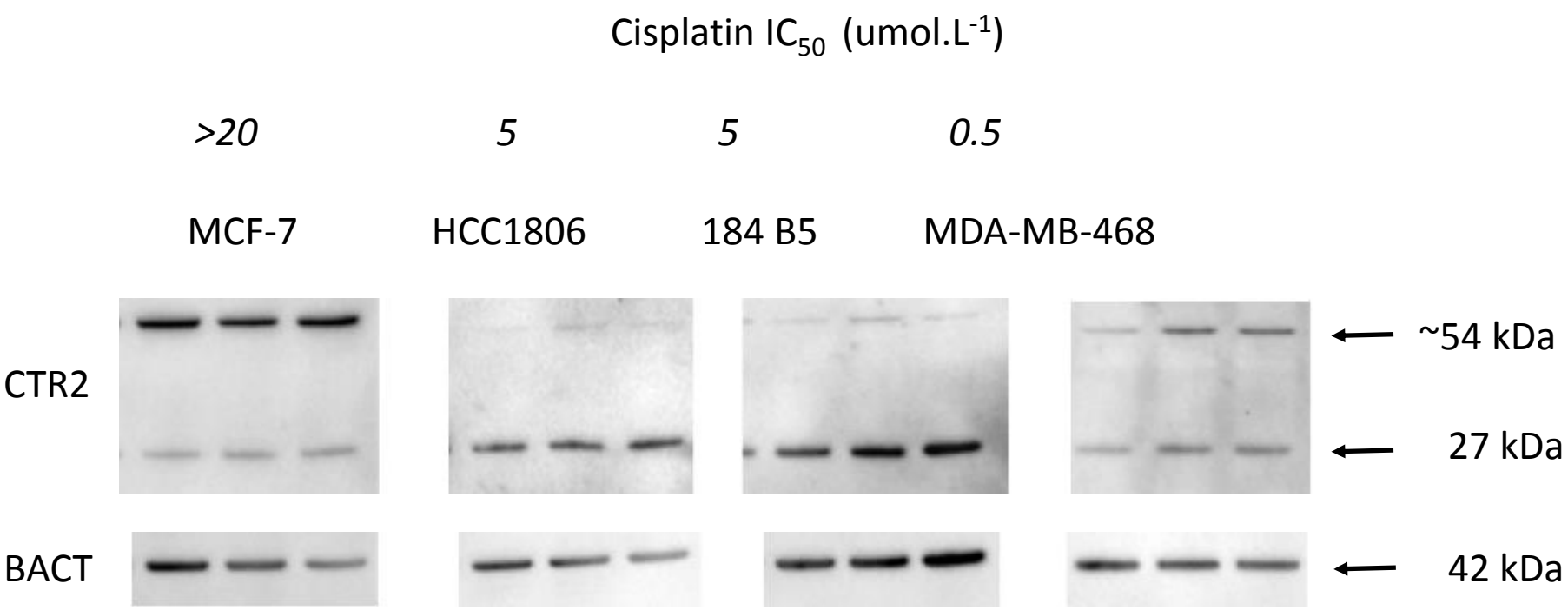


CTR2:CTR1 increased in BCa?

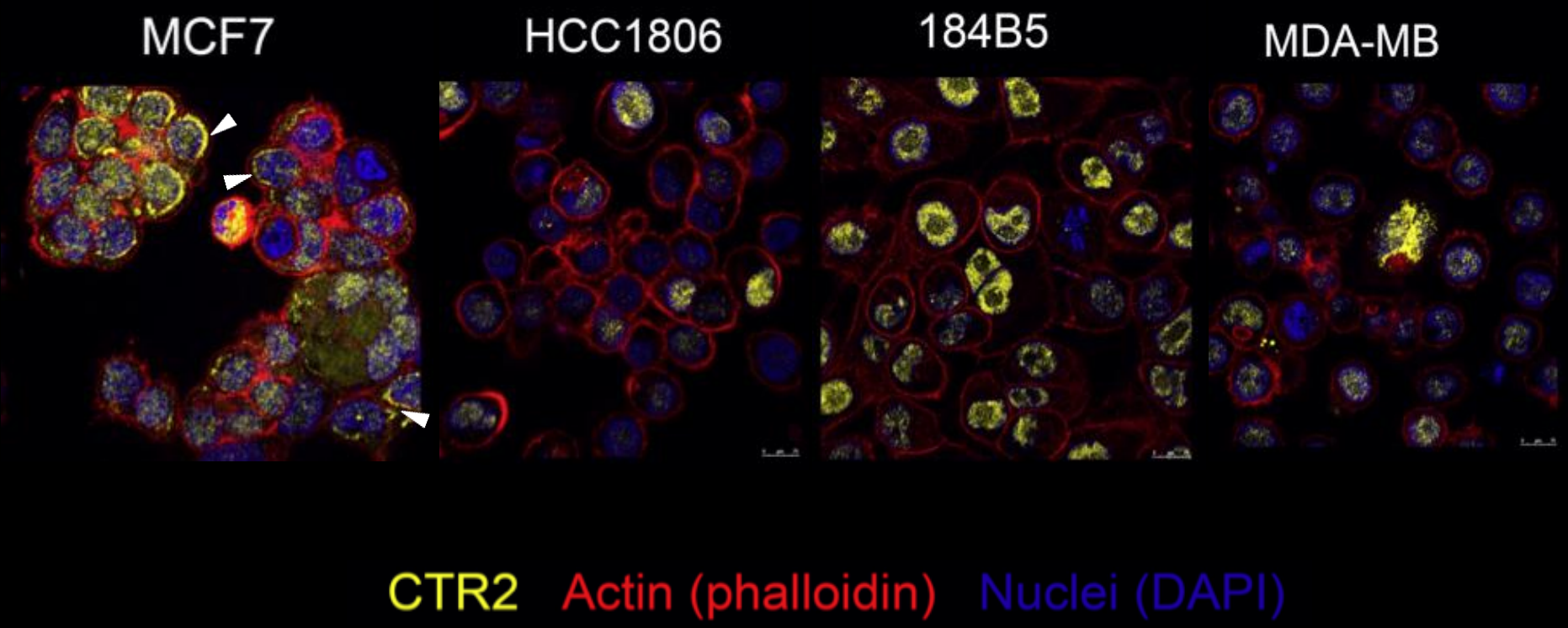




CTR2 dimer appears to determine sensitivity to cisplatin



CTR2 dimerisation appears to determine subcellular localisation



Conclusions

- Both CTR1 and CTR2 protein is decreased in breast cancer
- Greater levels of CTR2 appear to correlate with reduced cisplatin sensitivity
- Reduced cisplatin sensitivity is associated with CTR2 dimerisation and cytoplasmic localisation

Acknowledgements
Natalie Wee
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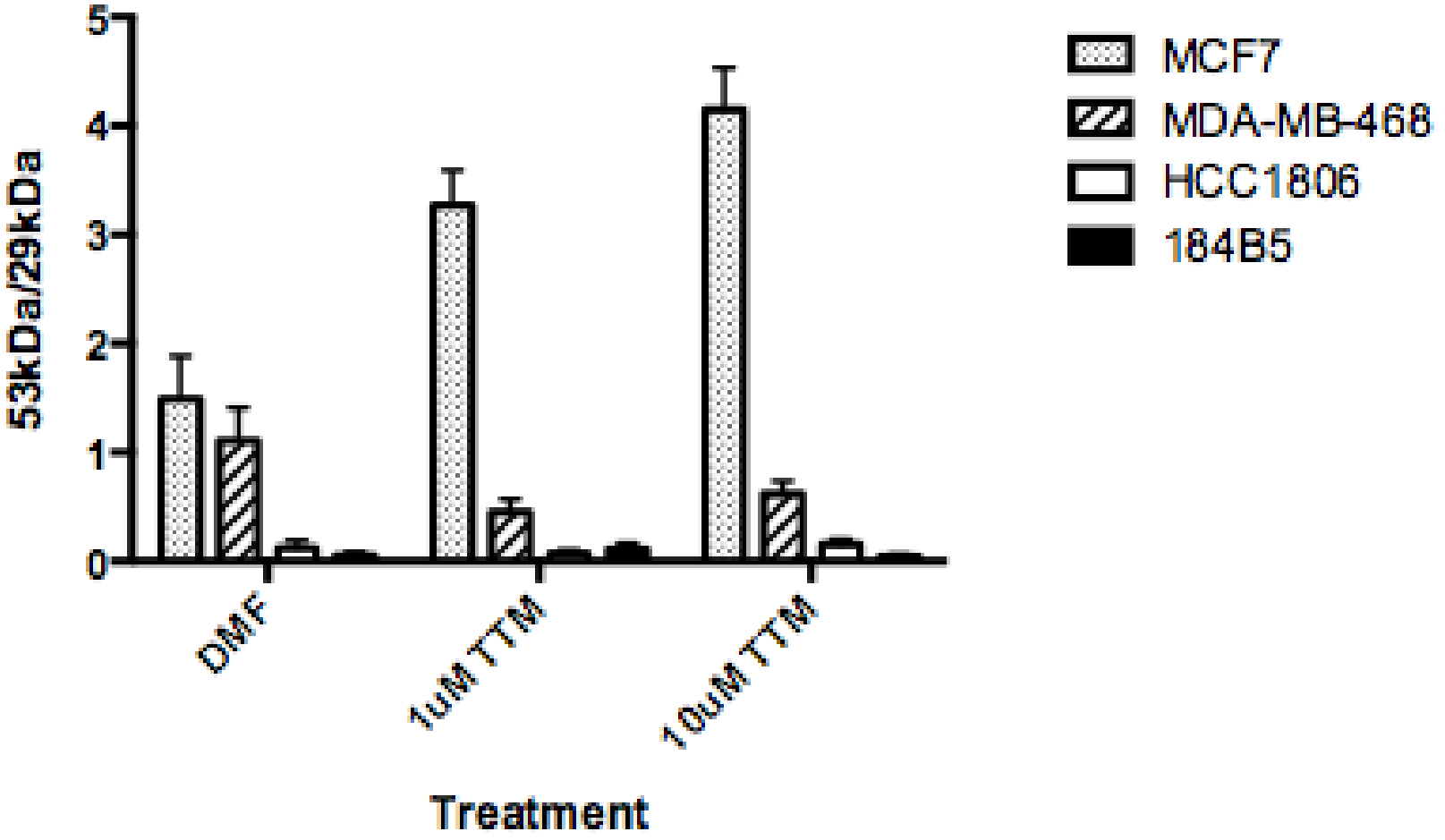
Dr Liz New (Dept. Chemistry, University of Sydney)

Bosch Translational Grant in Aid

Novel Concept Award


53kDa/29kDa
5
4
3
2
1
0
DMF
1uM TTM
10uM TTM
Treatment
MCF7
MDA-MB-468
HCC1806
184B5

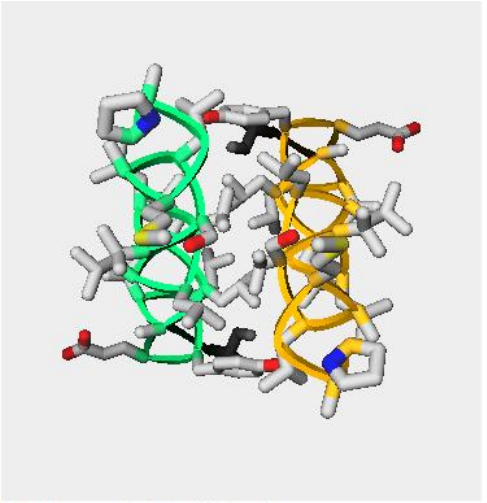
Prediction results for task: E7BBF693

Prediction results | Task details

Best models table for *pep-1_pep-2*. Click a table row to see corresponding 3D-structure and pair of MHP-maps.

Rank	F_{scor}	Crossing angle χ, deg	Rotation angle α_1, deg	Rotation angle α_2, deg
1	2.256	55.1	254	254
2	2.218	-4.9	104	98
3	1.771	-60	-22	-118
4	1.203	-35	8	-4
5	0.94	-29.8	200	200

You may download prediction results as files: Resulting table — Multi-pdb with models — Zip-archieve

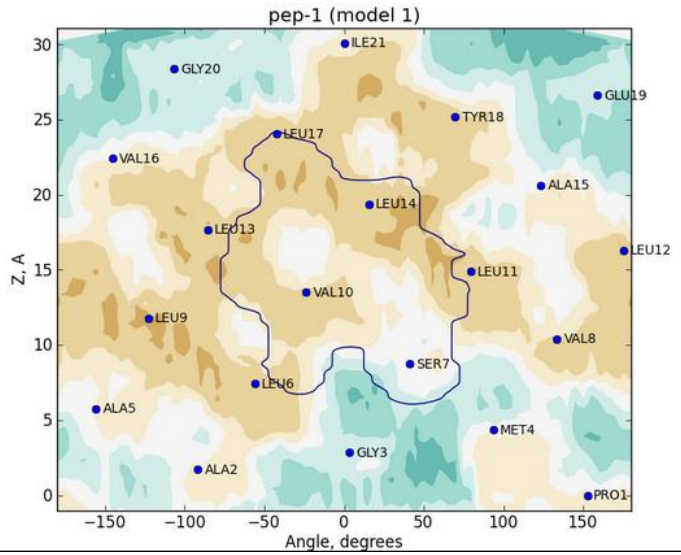


GLmol is used to show 3D structures.

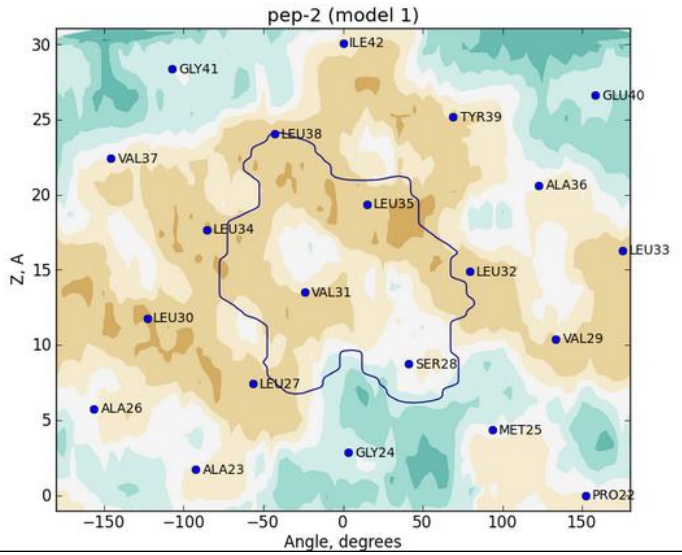
MHP-maps for *pep-1_pep-2 #1*

You may save maps as pictures or by clicking and saving vector pdf-versions.

Helix 1



Helix 2

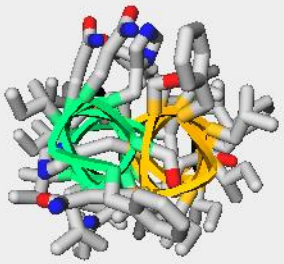


Prediction results for task: 2C96329C

Prediction results | Task details

Best models table for *pep-1_pep-2*. Click a table row to see corresponding 3D-structure and pair of MHP-maps.

Rank	F_{scor}	Crossing angle χ, deg	Rotation angle α_1, deg	Rotation angle α_2, deg
1	4.487	1.2	104	50
2	2.936	-60	158	158
3	2.882	45.2	182	182
4	1.724	-35.1	-52	-52
5	1.29	-5.1	-58	-46
6	1.166	55	368	368



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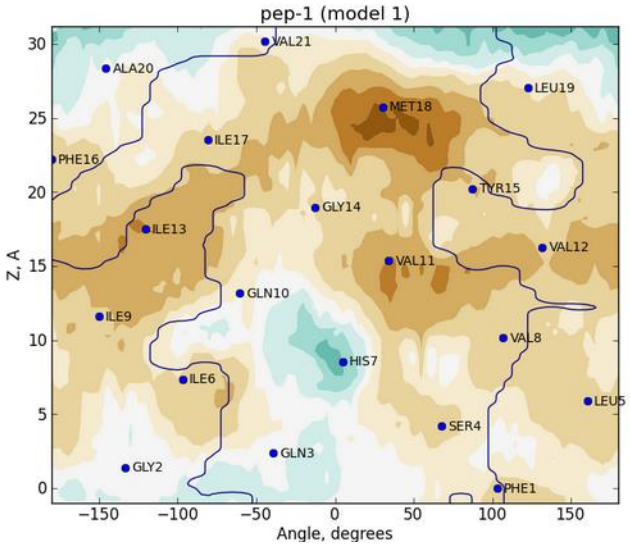

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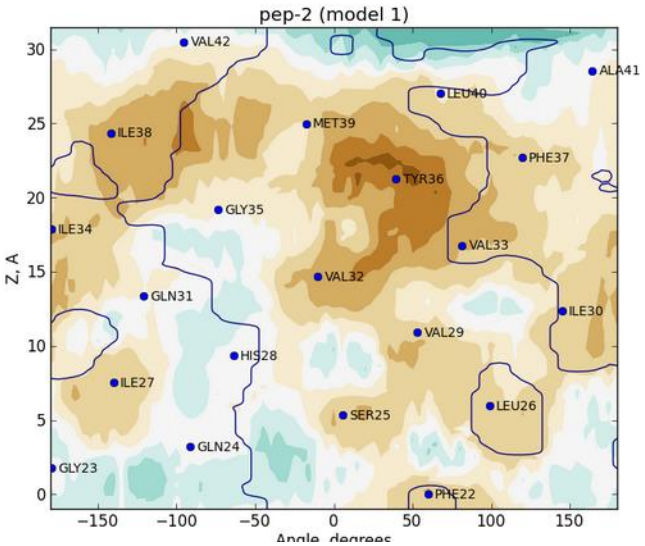


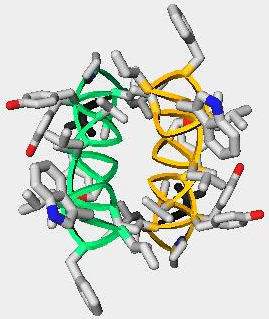
Prediction results for task: 21065E18

Prediction results | Task details

Best models table for *CTR2_TM3-1_CTR2_TM3-2*. Click a table row to see corresponding 3D-structure and pair of MHP-maps.

Rank	F_{scor}	Crossing angle χ, deg	Rotation angle α_1, deg	Rotation angle α_2, deg
1	3.68	-55	146	146
2	3.365	-15.9	212	212
3	3.084	55.2	344	338
4	2.639	10.9	302	302

You may download prediction results as files: Resulting table — Multi-pdb with models — Zip-archieve



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MHP-maps for *CTR2_TM3-1_CTR2_TM3-2 #1*

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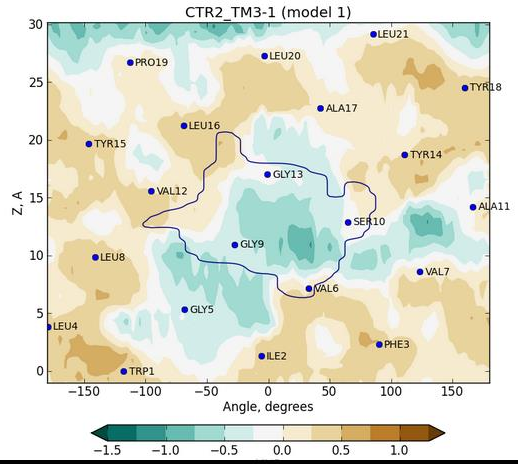

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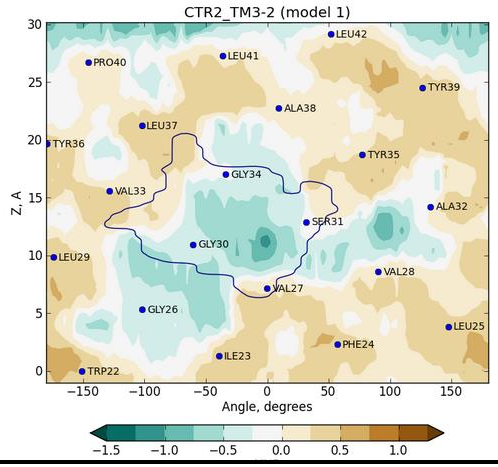

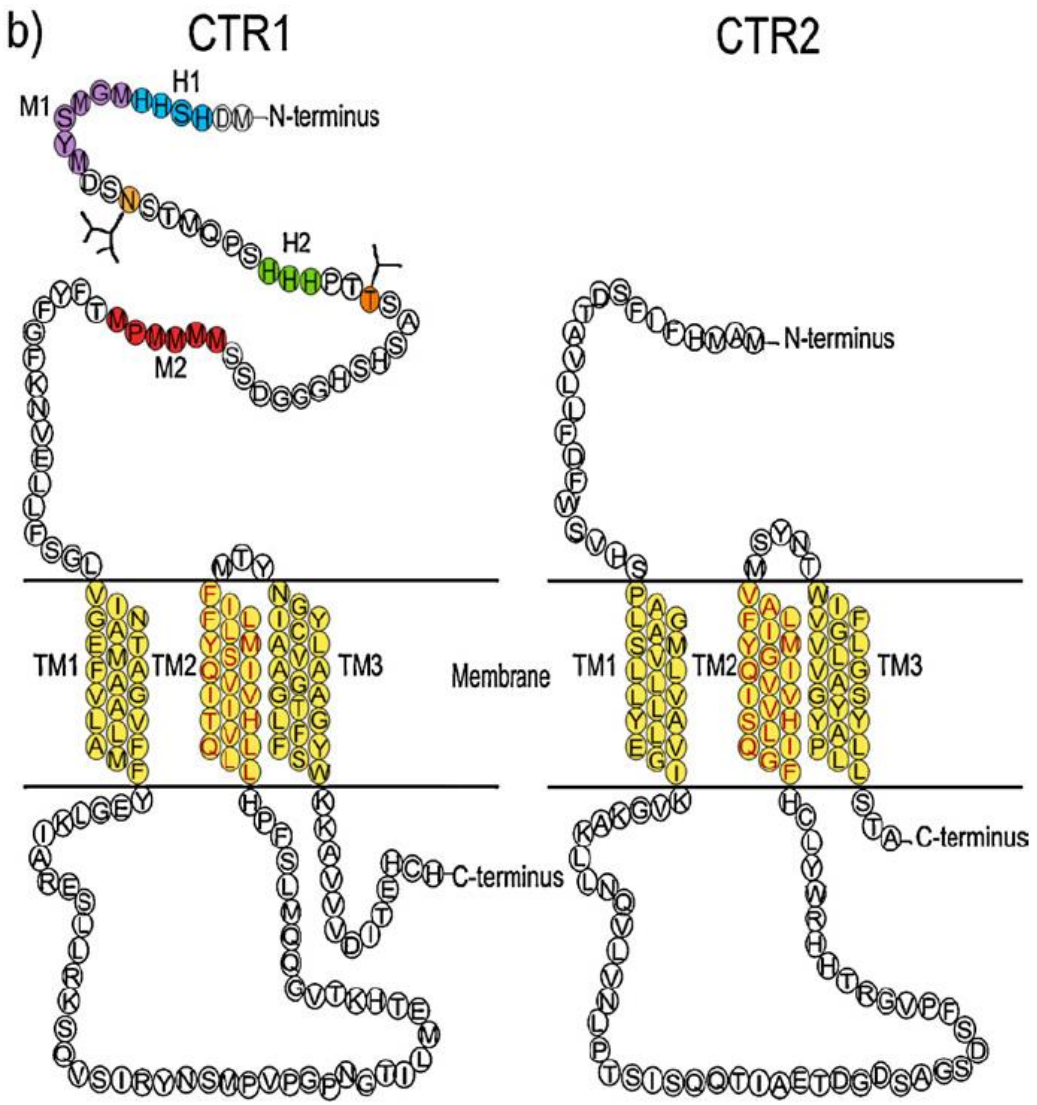

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