Regulation of Micronuclei in Human Breast Cancer Cells

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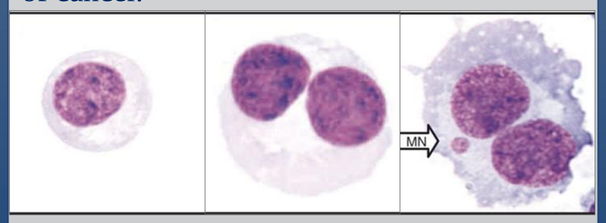
Introduction

Micronuclei (MN) are extra-nuclear bodies that contain damaged chromosome fragments or whole chromosomes that were not incorporated into the nucleus after an improper cell division. MN can be propagated by DNA damages, chromosome aberrations, and defect in the cellular repair mechanism. The presence of MN is important as an indicator for risk of cancer development and its malignancy because of its linear correlation with the genomic instability inside the cell. MN are induced by a variety of genotoxic substances or endocrine-disrupting chemicals that can disrupt genomic stability. Breast cancer is driven by estrogen hormones binding to the estrogen alpha-receptor, which potentiate cellular proliferation causing an abnormal growth. Endocrine-disrupting chemicals can mimic the effects of estrogen hormone, thus producing the same effect. As more cells undergo proliferation, more MN are produced causing aneuploidy, a condition in which the cells have an incorrect number of chromosomes, and is a characteristic in which many cancer imbues. The relationship of micronuclei formation and its MN-inducing substances can reflect the sensitivity in MN formation; potentially can be used as a biomarker for future prediction of cancer.



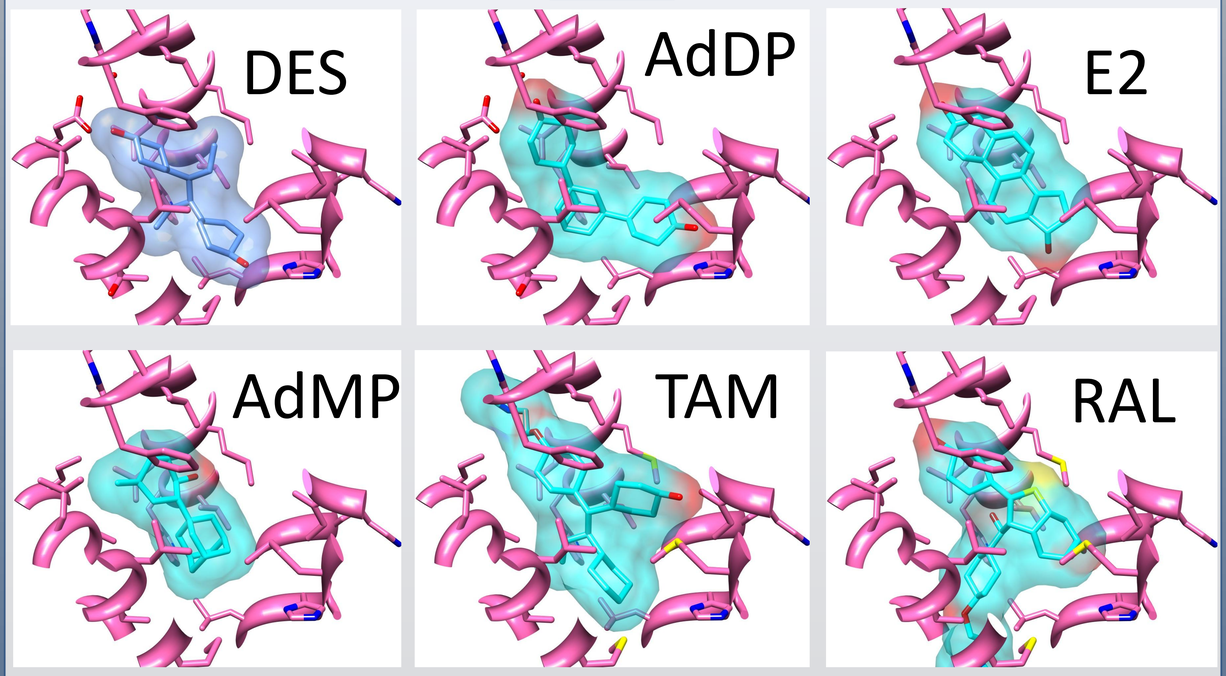
Objective

1. To establish the connection between estrogen-mimetic (endocrine-disrupting) compounds and its capability to induce Micronuclei.
2. To correlate the presences of Micronuclei and its relationship with risk of breast cancer.

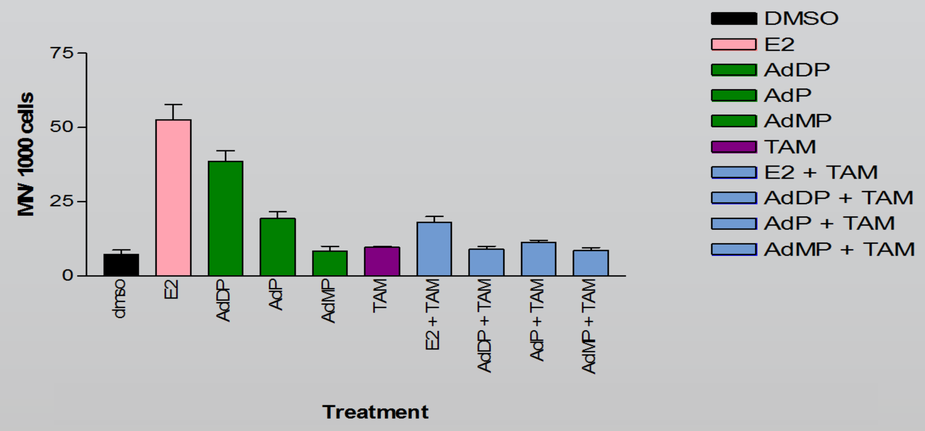
Method

Cytokinesis Block Micronucleus Assay to determine the quantitative measure of the micronucleus induced by exogenous estrogen compounds.

Results



	Total_Score	Crash	Polar	D_SCORE	PMF_SCORE	G_SCORE	CHEMSCORE	CSCORE
Diethylstilbestrol (**DES**)	7.96	-3.39	1.73	-137.8084	-26.8993	-270.4062	-33.6956	2
4-(1-Adamantyl) Phenol (**AdP**)	6.32	-2.09	1.94	-108.7842	-27.1218	-209.9703	-31.1973	2
Estradiol (**ES**)	6.25	-3.57	2.88	-126.4862	-35.903	-286.3802	-36.8231	2
2-(1-Adamantyl)-4- MethylPhenol (**AdMP**)	1.69	-4.81	0.01	-107.627	-19.9008	-228.8966	-30.058	2
4,4'-(1,3-Adamantanediyl)DiPhenol (**AdDP**)	-3.2	-14.2	0.03	-173.4735	-3.4836	-355.6393	-38.2222	3
Tamoxifene	-6.14	-19.9	0.81	-211.2945	4.7307	-415.7952	-44.7238	5
Raloxifene	-32.24	-45.9	1.6	-245.4505	120.1811	-463.8337	-58.8865	3



Formation of micronuclei after treatment with vehicle (0.1% DMSO), 1 nM estradiol and 5 uM each of AdDP, AdP and AdMP alone or in combination with 10 nM Tamoxifen. MCF-7 cells were cultured as described. After harvesting, cells were stained and analyzed microscopically as described in the methods section.

Conclusion

- Exposure to Estradiol induces higher concentration of Micronuclei.
- The presences of Micronuclei is associated with the occurrences of Breast Cancer.
- According to the docking score, compounds are that similar to Estradiol will act on the estrogen receptor and *may* produce the same effect to an extent; induction of Micronuclei and cell proliferation of cancerous cell.
- Anti-estrogenic compounds (ie. Tamoxifen and Raloxifene) prevents the increase of Micronuclei by preventing the cellular proliferation, thus decreasing the induction of Micronuclei.

References

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Future Perspectives

Future perspectives include experimentally accessing the severity of each compounds on the induction of micronuclei by quantifying the number of Micronuclei induced and to analyze the basic and the function of the 'proclaimed non-functional' Micronucleus.

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