Regulation of Micronuclei in Human Breast Cancer Cells

Kenny Wu1,2, Bethany K. Asare2, Rajendram V. Rajnarayanan Ph.D.2
1School of Medicine and Biomedical Sciences, 2Department of Pharmacology and Toxicology,
State University of New York at Buffalo, NY 14214

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.

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

Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Micronucleus Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES</td>
<td>7.94 ± 3.39</td>
</tr>
<tr>
<td>AdDP</td>
<td>6.23 ± 2.09</td>
</tr>
<tr>
<td>E2</td>
<td>5.62 ± 2.57</td>
</tr>
<tr>
<td>AdMP</td>
<td>4.81 ± 1.42</td>
</tr>
<tr>
<td>TAM</td>
<td>3.92 ± 1.42</td>
</tr>
<tr>
<td>RAL</td>
<td>2.24 ± 0.81</td>
</tr>
</tbody>
</table>

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

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.

Acknowledgements
I want to thank Dr. Rajnarayanan and Bethany Asare for assisting in my research project.