Determining the Effects of Soy-derived Isoflavones on Colorectal Cancer

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Background
Colorectal cancer (CRC) is one of the most predominant solid cancers in the Western world, accounting for an estimated 140,000 new cases, and 50,000 deaths in the US in 2018 (American Cancer Society, 2018). In general, it is metastatic disease which ultimately leads to mortality. Sporadic CRC and, therefore, mCRC development are strongly linked with aging (Nangia-Makker, et al., 2015). In an ever aging population, it is therefore essential that improved detection, treatment and, ideally, prevention strategies are put in place in order to combat CRC prevalence. It is known that the rate of CRC incidence is higher in developed nations, than in developing countries (Yu, et al., 2016) and there is a link between CRC incidence and genetic and environmental factors (Tárraga López, et al., 2014). Historically there has been a difference in CRC incidence between the Western world and Asian countries (Virk, et al., 2010). It is postulated that this could be due to a dramatic difference in the dietary intake of soy products. The incidence of CRC in Asian countries in increasing, attributed to the steady adoption of a Wester lifestyle, particularly in dietary habits (Deng, 2017). Epidemiological studies have shown that there is a 23% reduction in CRC risk following the consumption of soy isoflavones (Yu, et al., 2016). A significant protective effect from breast cancer has been shown in an Asian population, following the consumption of isoflavones & fermented soy products (Yamamoto, et al., 2003). Promising data on the protective nature of soy in regards to CRC exists: A meta-analysis by Yan et al., (2010) determined that there was no protective effect from soy on CRC for men, but there was for women; Spector et al., (2003) determined that, although study data had limitations, there was compelling evidence that soy could give some level of protection against CRC; A prospective study by Yang et al., (2009) showed a reduction in the risk of CRC in post-menopausal women following the consumption of soy foods. Limited data, however, is available on the potential of soy in reducing metastatic CRC (mCRC) risk. A study by Xiao et al., (2014) looked into changes in cancer cell invasiveness following in vitro exposure to genistein – a soy derived isoflavone. The study went on to show a reduction in mCRC in an in vivo study due to the intake of dietary genistein.

Aim
Within this research project, we will compare CRC cell lines and a metastatic CRC cell line. We will aim to determine the effects of the isoflavone genistein and its metabolically active glycoside, genistin,
along with Bowman-Birk protease inhibitor, on the viability, proliferative and invasive potential of the
cell lines.

**Methods**

Cell viability and proliferation will be assessed using a standard MTT assay. This assay allows us to
determine the toxic effects of compounds by determining the metabolic activity of viable cells through
the conversion of a tetrazolium dye into a formazan salt (Mosmann, 1983). Cell migration will be
assessed using a wound healing assay; this assay allows us to create a wound in the monolayer of the
cells, then assess the ability of the cells to heal the wound by migrating towards each other. Cell
invasion will be assessed using transwell assays; cells are seeded in a chamber adjacent to a
chemoattractant. Differences in invasion through the chamber following exposure to the soy
compounds will be assessed. PGE₂ levels are significantly increased in mCRC, compared with CRC
(Cianchi, et al., 2001). Alterations in PGE₂ protein levels due to exposure to the soy compounds will
be assed using western blotting techniques.

**Student Requirements**

As this is a predominantly cell culture based project, some experience with cell culture techniques
would be advantageous, although not essential as full training will be provided.

**Consumable Costs**

Please find below an estimated project cost, if all parts of the project are undertaken.

<table>
<thead>
<tr>
<th>Consumable</th>
<th>Approx cost</th>
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<tbody>
<tr>
<td>Genistein 5mg</td>
<td>£35</td>
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<tr>
<td>Genistin 1mg</td>
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<tr>
<td>BBI 10mg</td>
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<tr>
<td>Cell Culture reagents</td>
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<td>Cell Culture consumables</td>
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<tr>
<td>PGE₂ antibody 100µl</td>
<td>£320</td>
</tr>
</tbody>
</table>

**Total** £1000
References


Deng, Y., 2017. Rectal Cancer in Asian vs. Western Countries: Why the Variation in Incidence?. *Current Treatment Options in Oncology*.


