

TESTING OESTROGENICITY OF GLYPHOSATE

Breast Cancer UK is pleased to have awarded Dr Michael Antoniou from King's College London, research grants to evaluate the endocrine disrupting properties of the herbicide glyphosate, and to investigate the endocrine disrupting effects of low dose EDC mixtures of herbicides and bisphenol compounds. In March 2018, he and Dr Robin Mesnage (also from King's College London) were awarded further funding to evaluate the cancer-causing potential of bisphenol combinations in primary mammary epithelial cells.

Brief summary of Results

Glyphosate is oestrogenic at high concentration, but not at exposure levels normally encountered by the general population. Glyphosate-containing herbicides were not found to be oestrogenic.

Project description

Breast Cancer UK funded research carried out at King's College London, into the potential endocrine (hormone) disrupting effects of glyphosate and commercial glyphosate formulations.

Glyphosate-based herbicides (weedkillers) are the world's most abundantly used pesticides both in agriculture and domestically. Recently, WHO listed glyphosate as a probable cause of cancer in humans [1]. Glyphosate is not currently listed as an endocrine disrupting chemical (EDC), despite evidence [2], [3] which suggests it may interfere with oestrogen signaling that could lead to breast tumour formation and/or progression.

Human breast cancer cells, whose growth under laboratory conditions is either dependent or independent on the presence of oestrogen, will

be exposed to environmentally relevant (real world exposure) concentrations of glyphosate and commercial glyphosate formulations. Commercial glyphosate formulations are a mixture of glyphosate and a complex array of additional chemicals collectively labeled as “inert adjuvants” but which are proving to be toxic in their own right. Hence the need to test commercial glyphosate formulations alongside glyphosate alone. Cells will also be exposed to selective inhibitors of oestrogen receptors (e.g., tamoxifen) to determine their role in any toxic, endocrine disruptive effects observed. EDC effects will be determined by measuring cell survival, cell growth rates, and gene expression profiling (transcriptomic analysis), which provides insight into which biochemical pathways are affected.

This research will help advance our understanding of the potential dangers of glyphosate arising from EDC effects and how it interacts with oestrogen receptors to create a potentially carcinogenic environment, which may contribute to either the formation of breast cancer or stimulate its progression.

Description of results

Different glyphosate-based herbicide formulations, pure glyphosate, and co-formulant mixtures, were tested in cell culture systems using oestrogen-dependent and oestrogen independent human breast cancer cells, to determine whether compounds were able to mimic oestrogen-dependent or independent cell proliferation. Glyphosate was found to be a weak activator of the oestrogen receptor in hormone-dependent human breast cancer cells. Glyphosate formulations and co-formulants were not oestrogenic.

RNA sequencing and gene expression profiling using oestrogen-dependent human breast cells were used to assess involvement of other signaling pathways (including other non-classical oestrogenic pathways) and confirm any endocrine disruptive effects and computer modelling of the interaction of glyphosate at the active site of oestrogen receptor alpha was performed. The findings indicate that glyphosate does not bind to the oestrogen receptor alpha and is activating the receptor through a ligand-independent mechanism that may affect the balance between cell proliferation and programmed cell death.

References

1. [https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(15\)70134-8/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(15)70134-8/fulltext)
2. <https://www.ncbi.nlm.nih.gov/pubmed/17984146>
3. <https://www.ncbi.nlm.nih.gov/pubmed/23756170>