ABSTRACT

The role of the CLU (clusterin/Apo-J) gene in cancer genetics has been uncertain for over 20 years of research. While some studies suggest that CLU is an oncogene, others suggest that it inhibits tumorigenesis. Recent efforts in uncovering the function of CLU have reported its role in processes such as proliferation, apoptosis, and aggregation. It is believed that the elevated expression of CLU in humans may interfere with certain apoptotic pathways with isoforms of clusterin having differential effects. This meta-analysis assesses the effects of upregulating the intracellular form of CLU via expression vectors on cell proliferation as well as looking into intracellular clusterin’s involvement with tumorigenesis. Data compiled from recent studies suggests that intracellular clusterin activates survival in target cells by affecting cell cycle progression and activating a caspase-3 independent apoptotic mechanism which would allow cells to undergo cell death earlier than others resulting in decreased rate of cell proliferation and tumorigenesis.

INTRODUCTION

What is Clusterin?
- Plays numerous roles in cell function.
- Is a protein encoded on chromosome 8 in humans.
- Heavily expressed in the liver, brain, ovaries, and testes.
Clusterin in Alzheimer’s Disease and Cancers
- Clusterin is known to play a role in Alzheimer’s Disease.
- Linked with Cancer progression.
The Isoforms of Clusterin
- Intracellular clusterin is one of clusterin’s many isoforms.
- Role in cancer genetics has been uncertain for over 20 years.

RESULTS

Overall effect size was 0.51. 69% of the experimental group was below the mean of control group.

Large effect size: Strong relationship between variables. 69% overlap between variables.

HYPOTHESIS

Null Hypothesis: Upregulating CLU via expression vectors has no significant effect on cell proliferation and tumorigenesis.
Alternative Hypothesis: The upregulation of the intracellular CLU (Clusterin/Apo-J) by expression vectors decreases cell proliferation and tumorigenesis by inducing pro-apoptotic activities.

METHODOLOGY

Meta Analysis
- 5 studies, 6 data sets
- Inclusion/Exclusion Criteria
- Expression Vectors

METHODOLOGY

Assays and kits used to measure variables
- Intracellular CLU mRNA production: Northern Blot
- Cell count: Flow Cytometry analysis
- Presence of intracellular Clusterin: Western Blot/ Immunocytochemistry

STUDY

Study | Effect Size | % of Experimental group below the mean of control group

(Barrett, et al. 2002) | 0.57 | 75%
(Kim, et al. 2005) | 0.35 | 62%
(Sakurada, et al. 2004) | 0.71 | 70%
(Sakurada, et al. 2004) | 0.07 | 70-74%
(Sakurada, et al. 2004) | 0.55 | 70%
Overall | 0.31 | 65%

CONCLUSION

Potential Sources of error
- Mean and Standard Deviation not directly provided by study, calculated manually.
- The data collection period
- Access to full peer reviewed articles
Further Development of Study
- Replicate results in larger meta analysis
- Test effects of clusterin in different target cells/cell lines
- Inclusion and exclusion criteria should be modified to include studies that provide all statistical values.
Gene Therapy
- The use of intracellular clusterin to counteract the proliferative effect of clusterin.
- Counteract cancer development.

FURTHER STUDIES

REFERENCES