Bioactivity of a Novel Magainin Peptide, QUB-2392 on Human Leukaemia Lell lines.

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Background

- Despite advancements in cancer therapies, enhancing long-term survival rates for leukaemia patients and alleviating the adverse effects of conventional chemotherapy pose significant challenges.
- Apoptosis evasion plays a pivotal role in leukemogenesis, fuelling cancer progression [1]. This highlights the need for alternative anti-cancer agents that can selectively target cancer cells with minimal or no harm to healthy ones.
- For decades, research has highlighted the potential of bioactive peptides (BAPs) as anticancer agents, primarily through apoptosis induction. BAPs, sourced from natural origins represent a promising class of compounds with diverse bioactivities, including anticancer properties [2].

Aim

- This study focuses on a novel peptide, QUB-2392, a magainin peptide derived from amphibian skin secretions, examining its cytotoxic potential against human leukaemia cell lines, and exploring the underlying mechanisms of action (MOA).

Methods

- The study initially utilised MTS cell proliferation assay to assess the cytotoxic effect of QUB-2392 on four human leukaemia cell lines at 24- and 48-hour timepoints.
- To elucidate the mechanism of action (MOA), various molecular techniques were employed, including proteomics studies via mass spectrometry and gene profiling via RNA-sequencing, aimed at delineating alterations in protein and gene expression following treatment with QUB-2392 peptide.

Results

- The MTS assay indicated cytotoxicity across all tested cell lines, suggesting inhibition of cell growth. Proteomics studies revealed upregulation of pro-apoptotic proteins such as apoptosis-inducing factor, mitochondrial 1 (AIFM1), apoptotic chromatin condensation inducer in nucleus 1 (ACIN1), alongside downregulation of anti-apoptotic proteins like BCL-2.Gene profiling identified downregulated oncogenes like MYC, RUNXI, NOTCH 1 and NOTCH 2, and CEPBA, while upregulated genes, such as p53, were associated with tumour-suppressive activities.

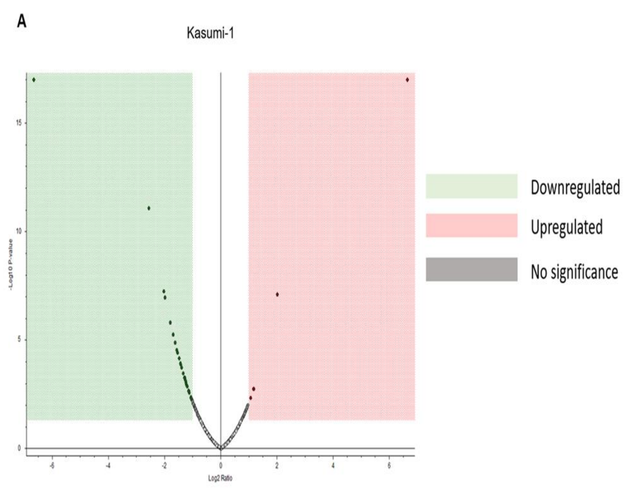

Figure 1*.Volcano plot showing upregulated proteins (pink zone) and downregulated proteins (green zone). (Dogwul, 2024).*

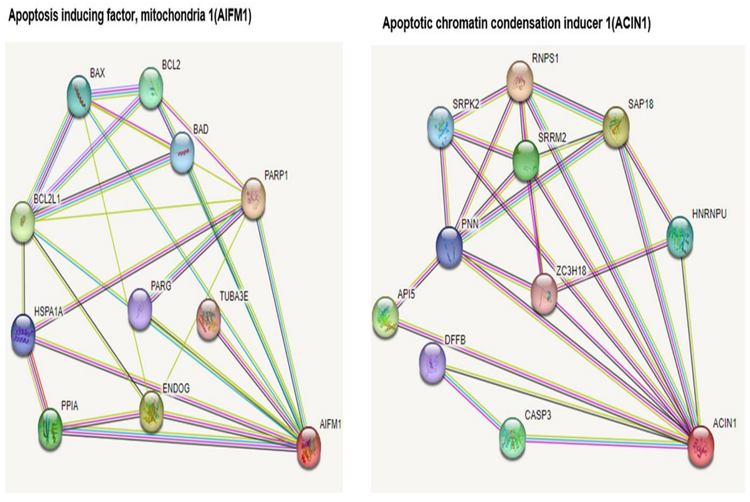

Figure 2*. AIFM1 and ACIN1 protein networks in MOLM-13 cells.*
Apoptosis-inducing factor, mitochondrial 1 (AIFM1) (left). Apoptotic chromatin condensation inducer in nucleus 1 (ACIN1 and) (right). Network nodes represent interconnected proteins. Associated protein networks are either complementing the parent protein or acting in antagonism (Dogwul, 2024).

Table 1. Key pro-apoptotic proteins with altered expression across the studied cell lines

Protein description	MOLM-13	Kasumi-1	Jurkat	K562
Apoptosis inducing factor, mitochondrion (AIFM)	↑	↑	↓*	↓
Apoptotic chromatin condensation inducer in nucleus 1 (ACIN1)	↑	↑	↓*	↑
Cytochrome-c (Cyt c)	↑	↑	↑	↑*
Cell cycle and apoptosis regulator 2(CCAR2)	↑	↑	↑	↑*
Apoptosis inhibitor	↓	↓	↑	↑*
B-cell lymphoma -2(BCL-2)	↓	↓	↓	↑*

↑ Upregulation ↓Downregulation * indicates up-or downregulated key proteins but no significance *(Dogwul, 2024).*

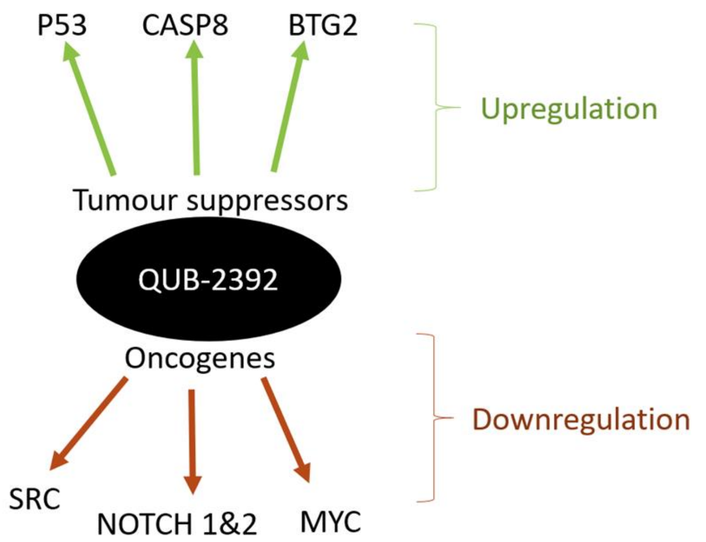

Figure 3. *QUB-2392 downregulates oncogenes while upregulating tumour suppressors (Dogwul, 2024).*

Abbreviations*: CASP8, caspase 8; P53, tumour protein p53; BTG2, BTG antiproliferation factor 2; SRC, sarcoma (Src) proto-oncogene; MYC, Myelocytomatosis (c-Myc) oncogene; NOTCH1, Neurogenic locus notch homolog protein 1.*

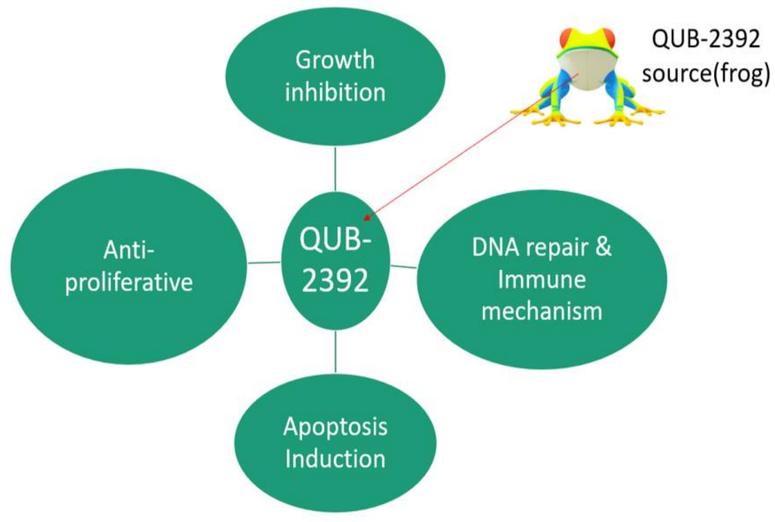

Figure 4. Anti-leukemic properties of QUB-2392 novel peptide *(Dogwul, 2024).*

Conclusion

- This study demonstrates the in vitro anti-leukemic activity of of the peptide, QUB-2392, highlighting its potential as a novel therapeutic agent. QUB-2392 induces apoptosis in the leukaemia cells and exhibits anti-proliferative, immunomodulatory, DNA repair, and tumour-suppressive properties. These findings suggest its promise as an anti-leukemic candidate warranting further investigations.

References

1. Adams, J. M., & Cory, S. (2018). The BCL-2 arbiters of apoptosis and their growing role as cancer targets. Cell Death and Differentiation, 25(1), 27–36. https://doi.org/10.1038/cdd.2017.161
2. Bechinger, B., & Gorr, S. U. (2017). Antimicrobial Peptides: Mechanisms of Action and Resistance. In Journal of Dental Research (Vol. 96, Issue 3, pp. 254–260). SAGE Publications Inc. https://doi.org/10.1177/0022034516679973
3. Dogwul, R.G. (2024*). Investigating the anti-leukemic effect of a novel bioactive peptide, QUB-2392 and the underlying mechanisms of action* [Unpublished PhD thesis].Middlesex University, London.