GANODERMA SPP. EXTRACTS FROM PUERTO RICO SHOW SELECTIVE ANTI-TRIPLE-NEGATIVE BREAST CANCER POTENTIAL

Gabrielle M. Silverio-Alvarado, BS1; Luz V. Arroyo-Cruz, PhD2; Sebastian Sagardia-González, BS3; Kart Miller, PhD3; Taotao Ling, PhD3; Fatima Rivas, PhD3; Michelle Martinez-Montemayor, PhD3
1Department of Biochemistry and Cancer Research Unit, Universidad Central del Caribe-School of Medicine, P.O. Box 60327 Bayamón, PR 00960-6032; 2Puerto Rico, Carolina, PR; 3Louisiana State University, Baton Rouge, LA

Abstract

Purpose

- Triple-negative breast cancer (TNBC) accounts for about 10-15% of all breast cancers diagnosed in people of color (e.g. Hispanics or African Americans). TNBC is characterized by the lack of hormone (ER & PR) and the epidermal growth factor receptor 2 (HER2), and there is an urgent clinical need for therapeutic approaches. The basidiomycete Ganoderma, has been used for medicinal purposes; including neotropical ones that are being deeply studied in TNBC models. The objective of this study is to identify the effects of neotropical native Ganoderma species found in Puerto Rico and test their efficacy in breast cancer cells. Native fractions extracted from Ganoderma multiplicatum (GMM; F1, F2, F3, F4, F6, F7) were tested against TNBC (SUM149) and non-cancerous mammary epithelial (MCF10A) cell lines. Methods: Cell viability assays were performed using increasing concentrations of different fractions ranging from 0 to 75 µM for 72h. After treatment, cell viability was determined by fluorescence detection (GloMax, Promega). Results: Our results indicate that SUM149 cancer cells have a significantly reduced viability in fractions F1, F2, F6, and F7. A greater significant inhibition concentration was detected for F7 (IC50 = 3.9 µM, F1 (IC50 = 8.4 µM) and F2 (IC50 = 13.3 µM). MCF10A non-cancerous cells results show only detectable inhibitory indexes for F1, F6 and F7 at IC50 of 497.9 µM, 15.41 µM and 1.166 µM, respectively. Conclusions: We conclude that fractions F1, F2 and F7 can be evaluated in more depth as fractions that might contain selective anti-TNBC bioactive compounds with great therapeutic potential.

Funding and Acknowledgements

The presenter of this poster would like to thank for their support:

- NIH/NCI, R01GM145488:
- USDANIAFARSBIR:
- Mercedes Lacourt

References

4. GMM: G. multiplicatum (GMM), G. lucidum (GLE), and G. tsugae (GTS).
5. G. multiplicatum.
6. G. lucidum.
7. G. tsugae.
8. G. multiplicatum.
10. G. tsugae.

Results

- Results of F4, F7, and F6 fractions. A and B) Fraction F4 (IC50 = 49.2 ± µM) and F7 (IC50 = 3.9 ± µM) showed efficient cellular inhibition on SUM149 cancer cells, and very low or no detectable inhibition on MCF10A. Student t-test analysis showed a significant difference (P < 0.01) and P = 0.0007 respectively; between the means of both cell lines, indicating a greater inhibitory effect on SUM149 compared to MCF10A. C) Fraction F6 displayed interesting results, which showed an opposite effect seen with the other evaluated fractions. F6 showed a decrease effect on MCF10A (IC50 = 107.95 ± µM) non-cancerous cells than in SUM149 (IC50 = 110.45 ± µM) Student t-test analysis showed a significant difference (P < 0.05) between the means of both cell lines.

Conclusions

- This study allowed the identification of the effects of native Ganoderma multiplicatum found in Puerto Rico and tested its efficacy in cancer and non-cancerous cell models.
- We showed that the F7 fraction had the lowest (IC50 = 3.9 µM) among all fractions evaluated in SUM149 TNBC cells, followed by F1 (8.4 µM) and F2 (11.3 µM).
- We conclude that from the fractions tested, fractions F1, F2, and F7 can be further evaluated as they might contain selective anti-TNBC bioactive compounds with great therapeutic potential.
- F6 showed greater toxicity against healthy cells.
- Our findings serve as a basis for further studies to elucidate the potential of G. multiplicatum as a therapeutic agent targeting TNBC.
- Future work would improve:
  - Characterizing G. multiplicatum extract mechanism of action;
  - Performing in vivo studies to test their effect in animal models;
  - Potentially studying the F6 fraction compounds and elucidate what makes this fraction so lethal to MCF10A noncancerous cells.

Figure 1: Five Main Molecular Breast Cancer Subtypes

Figure 2: G. multiplicatum and G. lucidum fractions against TNBC (SUM149) and non-cancerous mammary epithelial (MCF10A) cell line. (A) G. multiplicatum fractions inhibits SUM149 cells with a concentration of 15 µM; (B) G. lucidum fraction against MCF10A cells with a concentration of 20 µM. (C) Let-7a-3p up-regulation in SUM149 cells with concentrations of 5 µM.

Figure 3: Stages of cancer development (TNM). (A) T: tumor size, N: number of lymph nodes involved, M: metastasis. (B) TNM staging system: early stage 1, stage 2, stage 3, stage 4. (C) Stages of cancer development. (D) TNM staging system: stage 1, stage 2, stage 3, stage 4.

Figure 4: Results of F1, F2, and F3 fractions. A and B) Fraction F1 (IC50 = 8.4 µM) and F2 (IC50 = 11.3 µM) demonstrated efficient cellular inhibition on TNBC SUM149 cells and low or no cellular inhibition on MCF10A non-cancerous cells. C) The F3 fraction (IC50 = 40.4 µM) showed inhibition for SUM149 and no detectable inhibition for MCF10A. Student t-test analysis showed a significant difference (P < 0.002) between the compared means of both cell lines, indicating a greater inhibition of F3 in SUM149 cells compared to MCF10A.