Network Analysis on Cellular adhesion and Angiogenesis Genes of RAW 264.7 Macrophages as Affected by Lunasin Treatment

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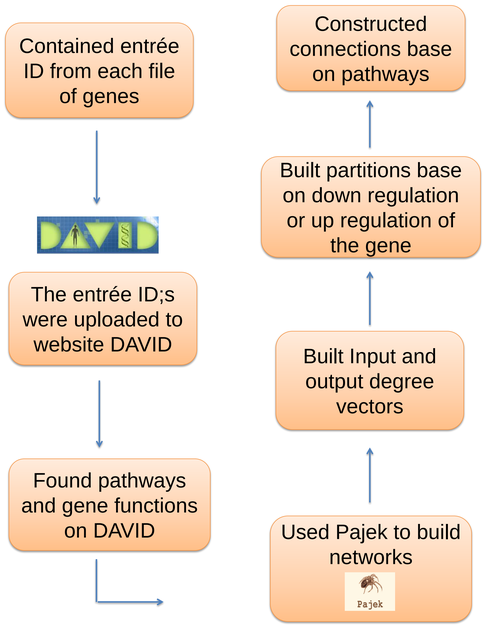
Abstract

Lunasin is a peptide with Arginine,-Glycine-Aspartic (RGD) acid motif associated with reducing the risk of developing certain chronic diseases such as cancer. We aimed to analyze cellular adhesion and angiogenesis genes of RAW 264.7 macrophages using computer software Pajek, and website DAVID affected by lunasin treatment. Analysis of genes showed that lunasin treatment affected pathways involved in ErbB signaling, p53 signaling and VEGF signaling. This result further confirm that lunasin will have an impact on genes associated with the process of cellular adhesion and angiogenesis which are important pathways involved in tumorigenesis.

Introduction

- Colorectal cancer (CRC) is the third most common cancer in the United states in men and women.
- Lunasin is a soy peptide composed of 43 amino acids that contains a unique Arg-Gly-Asp (RGD) amino acid motif.
- Pajek is computer software for analysis and visualization of very large networks and was developed in November of 1996.
- The objective of this study is to identify key regulatory pathway involved in cellular adhesion and angiogenesis affected by lunasin treatment in RAW 264.7 macrophages using Pajek Network Analysis Software.

Materials and Methods



Results

Gene symbol	Gene description	List ID	Fold Change (p-value) DvsA (Lunasin alone)
Areg	Amphiregulin	NM_009704	-2.2 (< 0.001)
Camk2d	Calcium/Calmodulin-Dependent Protein	N/A	-2.9 (< 0.001)
Ccne2	cyclin E2	NM_009830	7.8 (< 0.001)
Cdk2	cyclin-dependent kinase 2	NM_183417	2.2 (< 0.001)
Cdkn1a	Cyclin-Dependent Kinase Inhibitor 1A	NM_001111099	-1.8 (< 0.001)
Chek2	checkpoint kinase 2	NM_016681	2.3 (< 0.001)
Gadd45b	growth arrest and DNA-damage-inducible, beta	NM_008655	-8.7(< 0.001)
Gadd45g	growth arrest and DNA-damage-inducible, gamma	NM_011817	-4.4 (< 0.001)
Hbegf	Heparin-Binding EGF-Like Growth Factor	NM_010415	-4.2 (< 0.001)
Hras1	Transforming protein p21	NM_008284	1.6 (< 0.001)
Mapk14	Mitogen-Activated Protein Kinase 14	NM_011951	1.5 (< 0.001)
Mapkapk3	Mitogen-Activated Protein Kinase-Activated Protein Kinase 3	NM_178907	-6.3 (< 0.001)
Nfatf5	Nuclear Factor Of Activated T-Cells 5, Tonicity-Responsive	N/A	2.5 (< 0.001)
Nfatc1	Nuclear Factor Of Activated T-Cells, Cytoplasmic, Calcineurin-Dependent 1	NM_198429	5.7 (<0.001)
Nos3	Nitric Oxide Synthase 3	NM_008713	-2.7 (< 0.001)
Pak2	P21 Protein (Cdc42/Rac)-Activated Kinase 2	NM_177326	1.9 (< 0.001)
Pik3r1	Phosphoinositide-3-Kinase, Regulatory Subunit 1 (Alpha)	NM_001077495	1.8 (< 0.001)
Pik3r2	Phosphoinositide-3-Kinase, Regulatory Subunit 2 (Beta)	NM_008841	2.2 (< 0.001)
Pik3r5	Phosphoinositide-3-Kinase, Regulatory Subunit 5	N/A	-4.5 (< 0.001)
Ppm1d	Protein Phosphatase, Mg2+/Mn2+ Dependent, 1D	NM_016910	4.5 (< 0.001)
Sh2d2a	SH2 Domain Containing 2A	NM_021309	-5.6 (< 0.001)
Siah1b	Siah E3 Ubiquitin Protein Ligase 1 beta	NM_009173	2.4 (< 0.001)

Table 1. Genes from file DsvA , which is the treatment group with Lunasin only

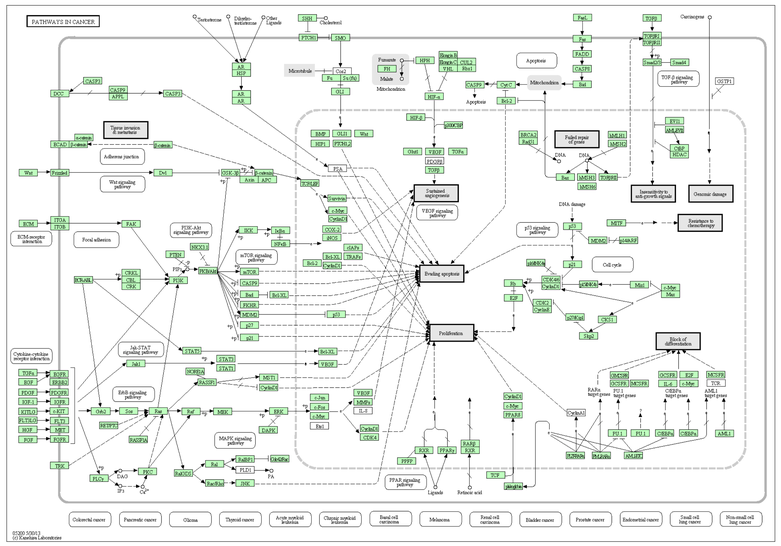


Figure 1. Pathways in Cancer, including Vascular endothelial growth factor (VEGF), Protein 53 (P53), and epidermal growth factor receptor (ErbB) signaling pathways found on DAVID website.

Epidermal growth factor receptor Signaling Pathway

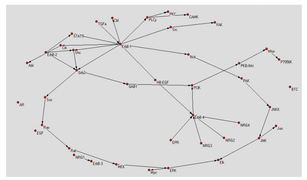


Figure 1. Epidermal growth factor receptor Signaling Pathway Network

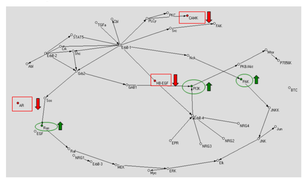


Figure 2. Epidermal growth factor receptor Signaling Pathway partition

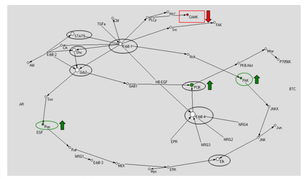


Figure 3. Epidermal growth factor receptor signaling pathway input degree vector

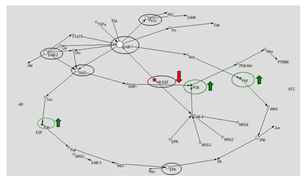


Figure 4. Epidermal growth factor receptor signaling pathway output degree vector

Protein 53 Signaling Pathway

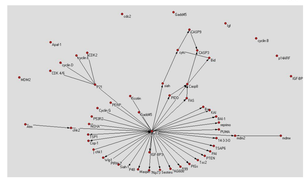


Figure 5. Protein 53 Signaling Pathway Network

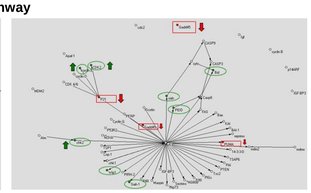


Figure 6. Protein 53 signaling pathway partition

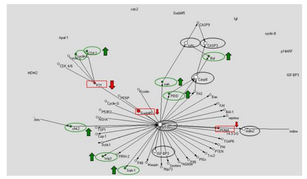


Figure 7. Protein 53 Signaling Pathway input degree vector

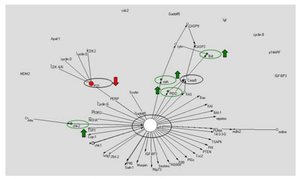


Figure 8. Protein 53 Signaling Pathway output degree vector

Vascular endothelial growth factor Signaling Pathway

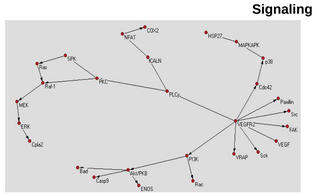


Figure 9. Vascular endothelial growth factor Signaling Pathway network

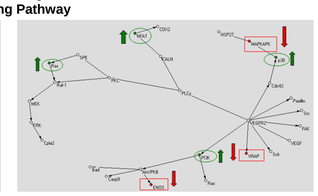


Figure 10. Vascular endothelial growth factor signaling pathway partition

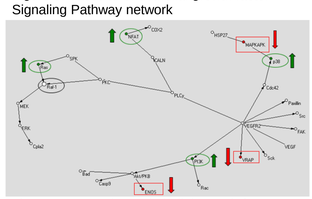


Figure 11. Vascular endothelial growth factor Signaling Pathway input degree vector

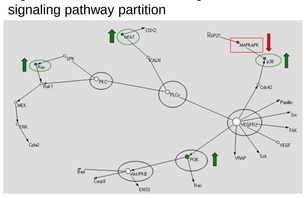


Figure 12. Vascular endothelial growth factor Signaling Pathway output degree vector

Conclusions

- Lunasin affected genes associated with cellular growth and proliferation, and angiogenesis in epidermal growth factor receptor (ErbB), protein 53 (P53), and in vascular endothelial growth factor (VEGF) signaling pathways.
- Cellular adhesion and angiogenesis genes affected by lunasin treatment changed signaling pathway function (VEGF, P53, and ErbB).
- Genes that were either upregulated or downregulated affected final function in the pathways such as cell proliferation and eventually lead to affecting cancer development.
- Consumption of soy may be useful to prevent comorbidities such as cancer.

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