



SCIENTIFIC PAPER | VOLUME 186, ISSUE 5, P552-555, NOVEMBER 01, 2003

Keyhole limpet hemocyanin, a novel immune stimulant with promising anticancer activity in Barrett's esophageal adenocarcinoma

David W McFadden, M.D.   • Dale R Riggs • Barbara J Jackson • Linda Vona-Davis, Ph.D.DOI: <https://doi.org/10.1016/j.amjsurg.2003.08.002>

Abstract

Background

Keyhole limpet hemocyanin (KLH) is a recently described immune stimulant and hapten carrier derived from a circulating glycoprotein of the marine mollusk *Megathura crenulata*. We previously reported that KLH has significant antiproliferative effects *in vitro* against breast, pancreas, and prostate cancers. We hypothesized that KLH would be effective against Barrett's esophageal adenocarcinoma in an *in vitro* model.

Methods

Barrett's esophageal adenocarcinoma cell lines (SEG-1 and BIC-1) were cultured using standard techniques. Cells were plated at 1×10^5 and KLH was added at concentrations ranging from 400ng to 100µg/well. After 24 and 72h incubation, cells were assayed for viability using the MTT technique. Statistical analysis was performed using ANOVA. Apoptosis was evaluated using a cell death detection kit after 16 hours of incubation with KLH.

KLH treatment significantly ($p < 0.001$) reduced viability in a dose and time-dependent manner. Apoptosis was increased in treated SEG-1 cells, but no changes in apoptosis were seen in treated BIC-1 cells.

Conclusions

KLH directly inhibits the growth of human Barrett's esophageal cancer *in vitro* by apoptotic and nonapoptotic mechanisms.

Keywords

[Keyhole limpet hemocyanin](#) • [Esophageal cancer](#) • [Barrett's esophagus](#) • [Apoptosis](#)

To read this article in full you will need to make a payment

[Purchase one-time access](#)

[Subscribe to *The American Journal of Surgery*](#)

Already a print subscriber? [Claim online access](#)

Already an online subscriber? [Sign in](#)

Register: [Create an account](#)

Institutional Access: [Sign in to ScienceDirect](#)

References

1. Riggs D.R. • Jackson B. • Vona-Davis L. • McFadden D.
vitro anticancer effects of a novel immunostimulant.
Surg Res. 2002; **108**: 279-284

[View in Article](#) ^[Scopus \(38\)](#) • [PubMed](#) • [Abstract](#) • [Full Text PDF](#) • [Google Scholar](#)

2. Harris J.R. • Markl J.

Keyhole limpet hemocyanin.

Eur Urol. 2000; **37**: 24-33

[View in Article](#) ^[Scopus \(62\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

3. Tzianabos A.O.

Polysaccharide immunomodulators as therapeutic agents.

Clin Microbiol Rev. 2000; **13**: 523-533

[View in Article](#) ^[Scopus \(493\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

4. Olsson C.A. • Chute R. • Rao C.N.

Immunologic reduction of bladder cancer recurrence rate.

J Urol. 1974; **111**: 173-176

[View in Article](#) ^[Scopus \(56\)](#) • [PubMed](#) • [Abstract](#) • [Full Text PDF](#) • [Google Scholar](#)

5. Riggs D.R. • Tarry W.F. • DeHaven J.I. • et al.

Immunotherapy of murine transitional cell carcinoma of the bladder using alpha and gamma interferon in combination with other forms of immunotherapy.

J Urol. 1992; **147**: 212-214

[View in Article](#) ^[PubMed](#) • [Google Scholar](#)

6. Brincic-Winkler C.D. • Metz K.A. • Beuth J. • Klippel K.F.

Keyhole limpet hemocyanin for carcinoma in situ of the bladder.

Eur Urol. 2000; **37**: 45-49

[View in Article](#) ^

[Scopus \(41\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

7. Jurincic-Winkler CD, von der Kammer H, Beuth J, et al. Antibody response to keyhole limpet hemocyanin (KLH) treatment in patients with superficial bladder carcinoma. *Anticancer Res* 1996;16:2105–10

[View in Article](#) ^

[Google Scholar](#)

8. Lamm D.L. • DeHaven J.I. • Riggs D.R.
Keyhole limpet hemocyanin immunotherapy of bladder cancer.
Eur Urol. 2000; **37**: 41-44

[View in Article](#) ^

[Scopus \(58\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

9. DeMeester T.R.
Barrett's esophagus.
Surgery. 1993; **113**: 239-241

[View in Article](#) ^

[PubMed](#) • [Google Scholar](#)

10. Streitz J.M. • Ellis F.H. • Gibb S.P. • et al.
Adenocarcinoma in Barrett's esophagus. A clinicopathologic study of 65 cases.
Ann Surg. 1991; **213**: 122-125

[View in Article](#) ^

[Scopus \(127\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)



Ann Thorac Surg. 1990; **49**: 537-541

[View in Article](#) ^

[Scopus \(167\)](#) • [PubMed](#) • [Abstract](#) • [Full Text PDF](#) • [Google Scholar](#)

12. Devesa S.S. • Blot W.J. • Fraumeni J.F.

Changing patterns in the incidence of esophageal and gastric carcinoma in the United States.

Cancer. 1998; **83**: 2049-2053

[View in Article](#) ^

[Scopus \(1897\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

13. Soldes O.S. • Kuick R.D. • Thompson I.A. • et al.

Differential expression of Hsp27 in normal oesophagus, Barrett's metaplasia and oesophageal adenocarcinomas.

Br J Cancer. 1999; **79**: 595-603

[View in Article](#) ^

[Scopus \(102\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

14. Mosmann T.

Rapid colorimetric assay for cellular growth and survival.

J Immunol Meth., 1983; **65**: 55-63

[View in Article](#) ^

[Scopus \(41468\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

15. Ludbrook J.

Multiple comparison procedures updated.

Clin Exp Pharmacol Physiol. 1998; **25**: 1032-1037

[View in Article](#) ^

[opus \(440\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)



16. Lamm D.L. • DeHaven J.I. • Riggs D.R. • Ebert R.F.

Immunotherapy of murine bladder cancer with keyhole limpet hemocyanin (KLH).

J Urol. 1993; **149**: 648-652

[View in Article](#) ^

[Scopus \(24\)](#) • [PubMed](#) • [Abstract](#) • [Full Text PDF](#) • [Google Scholar](#)

17. Thompson C.B.

Apoptosis in the pathogenesis and treatment of disease.

Science. 1995; **267**: 1456-1462

[View in Article](#) ^

[Scopus \(5918\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

18. Martin K. • Kirkwood T.B. • Potten C.S.

Age changes in stem cells of murine small intestinal crypts.

Exp Cell Res. 1998; **241**: 316-323

[View in Article](#) ^

[Scopus \(93\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

19. Tsai T.T. • Bongiorno P.F. • Orringer M.B. • Beer D.G.

Detection of p53 nuclear protein accumulation in brushings and biopsies of Barrett's esophagus.

Cancer Detect Prev. 1997; **21**: 326-331

[View in Article](#) ^

[PubMed](#) • [Google Scholar](#)

20. Souza R.F. • Shewmake K. • Beer D.G. • et al.

Selective inhibition of cyclooxygenase-2 suppresses growth and induces apoptosis in human esophageal adenocarcinoma cells.

Cancer Res. 2000; **60**: 5767-5772



[View in Article](#) ^

[PubMed](#) • [Google Scholar](#)

21. Jemal A. • Murray T. • Samuels A. • et al.
Cancer statistics, 2003.
CA Cancer J Clin. 2003; **53**: 5-26

[View in Article](#) ^

[Scopus \(3307\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

Article Info

Publication History

Received in revised form: July 16, 2003
Received: June 2, 2003

Identification

DOI: <https://doi.org/10.1016/j.amjsurg.2003.08.002>

Copyright

© 2003 Elsevier Inc. Published by Elsevier Inc. All rights reserved.

ScienceDirect

[Access this article on ScienceDirect](#)

Contact Information	Reprints	Surgical Education	Surgical Association	General Information on Society Sponsors
Editorial Board	New Content Alerts	Association of Women Surgeons	Society of Black Academic Surgeons (SBAS)	MORE PERIODICALS
Info for Advertisers	Subscribe	Midwest Surgical Association	Southwestern Surgical Congress	Find a Periodical
Pricing	SOCIETY INFORMATION	North Pacific Association for		Go to Product Catalog

We use cookies to help provide and enhance our service and tailor content and ads. By continuing you agree to the [Use of Cookies](#).

Copyright © 2021 Elsevier Inc. except certain content provided by third parties.

[Privacy Policy](#) [Terms and Conditions](#) [Accessibility](#) [Help & Contact](#)

