HCG (human chorionic gonadotropin) References

1. Beard J. The Unitarian trophoblastic theory of cancer. *Lancet*. 1902;1:1758.

2. Navarro M. 72nd Sci Meeting of the Cavite Med Soc; 1959;Trece Martires City, Philippines.

3. Williams RR, McIntire KR, Waldmann TA, et al. Tumor-associated antigen levels (CEA, HCG, alpha-feto protein) antedating the diagnosis of cancer in the Framingham study. *J Natl Cancer Inst*. 1977 June;58(6):1547–1551. http://www.ncbi.nlm.nih.gov/pubmed/68118

4. Fujimoto S, et al. The presence of an aberrant type of human chorionic gonadotropin in patients with gastric or colorectal cancer. *Jpn J Surg.* 1987 Sep;17(5):382–387. http://www.ncbi.nlm.nih.gov/pubmed/2448514

5. Acavedo HF, et al. Flow cytometry method for the analysis of membrane-associated HCG, its subunits and fragments on human cancer cells. *Cancer*. 1992 Apr 1; 69(7):1818–1828. http://www.ncbi.nlm.nih.gov/pubmed/1372527

6. Marcillac I, et al. Free human chorionic gonadotropin β subunit in gonadal and nongonadal neoplasms. *Cancer Res*. 1992 Jul 15; 52(14):3901–3907. http://www.ncbi.nlm.nih.gov/pubmed/1377600

7. Acavedo HF, et al. HCG-β gene expression in cultured human fetal and cancer cells of different types of origins. *Cancer*. 1995 Oct 15; 76(8):1467–1475. http://www.ncbi.nlm.nih.gov/pubmed/8620425

8. Birken S, et al. Isolation and characterization of human pituitary chorionic gonadotropin. *Endocrinol.* 1996 Apr; 137(4):1402–1411. http://www.ncbi.nlm.nih.gov/pubmed/8625917

9. Sheaff MT, et al. β-HCG as a prognostic marker in adenocarcinoma of the prostate. *J Clin Pathol*. 1996 Apr; 49(4):329-332. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC500461/

10. Guo S, et al. Effect of HCG in the gene expression profile of MCF-7 cell. *Int J Oncol*. 2004 Feb:24(2):399-407. http://www.ncbi.nlm.nih.gov/pubmed/14719117
    There are "48 genes that are affected by this hormone."

11. Huhtaniemi I, et al. Multiple sites of tumorigenesis in transgenic mice over producing HCG. *Mol Cell Endocrinol*. 2005 Apr 29; 234(1-2):117-126. http://www.ncbi.nlm.nih.gov/pubmed/15836960

    "….prolonged overexpression of HCG in adults, particularly in women, has been linked to the development of tumors e.g. gestational trophoblastic diseases, choriocarcinoma/germ cell tumors, osteosarcoma, bladder cancer, and prostate cancer."

12. Martinez Flores A, et al. Development and validation of an in vitro culture model for the study of the differentiation of human trophoblast. [In Spanish.] *Ginecol Obstet Mex*. 2006 Dec;74(12):657–665. http://www.ncbi.nlm.nih.gov/pubmed/17539321

13. Bjurlin MA, et al. Histologically pure stage I seminoma with an elevated beta-HCG of 4497 IU/l. *Urology*. 2007 Nov; 70(5):1007.e13–5. http://www.ncbi.nlm.nih.gov/pubmed/18068467

14. Akhvlediani L, et al. Detection of tolerance against HCG at malignant and benign tumors of female reproduction system. *Georgian Med News*, 2009 June; 171:20-24.

    "In case of malignant tumors as auto-antibody concentration is low and HCG level is high, HCG plays a role of autocrine growth factor for tumor cells and maintains the malignancy and tumor growth. The existence of auto-antibody indicates that the immune system is not completely tolerant to HCG"

15. Schandl, EK. The cancer profile and its clinical applications, *Townsend Letter*. 2010 August/September; pages 84-86. http://townsendletter.com/AugSept2010/cancerprofile0810.html

16. Cole LA, et al. USA HCG reference service, 10-year report. *Clin Biochem*. 2010 Aug;43(12):1013-22.

PHI (phosphohexose isomerase) References

1. Munjal, D, et al. CEA and PHI, GGT and LDH levels in patients with and without liver metastases. *Cancer,* 1976 April; 37:1800-1807. http://www.ncbi.nlm.nih.gov/pubmed/4219

   "Several investigators have reported that serum PHI is often elevated in cancer of the gastrointestinal tract (G.I.), head, neck and esophagus, lung and breast; and many years ago Bodansky and others considered the PHI levels to be the best "index" of malignancy in cancer patients"

2. Schandl, E K. Clinical biochemical parameters in cancer diagnosis and therapy. *Clinical Chemistry*, 1980; 26(7): 1040.

3. Baumann, M, et al. The diagnostic validity of the serum tumor marker phosphohexose isomerase (PHI) in patients with gastrointestinal, kidney, and breast cancer. Institute of Biochemistry Medical Faculty, Federal Republic of Germany, 1990 Vol. 8, No. 3-4 , Pages 351-356 http://informahealthcare.com/doi/abs/10.3109/07357909009012053

4. Silletti S, Raz A. Autocrine motility factor is a growth factor. *Biochem Biophys Res Commun.* 1993 July 15; 194 (1): 446-57. http://www.ncbi.nlm.nih.gov/pubmed/8392842

   "This is the first report of the paracrine and mitogenic actions of AMF and the results presented here show that AMF functions as a growth factor and suggest a possible role for its activity in normal tissue regeneration and tumor cell dissemination"

5. Watanabe, H, et al. Tumor cell AMF is the neuroleukin/phosphohexose isomerase polypeptide. *Am Assoc Cancer Res J*; 1996 http://cancerres.aacrjournals.org/content/56/13/2960

"The structure of the autocrine motility factor (AMF), a tumor secreted cytokine which stimulates cell migration in vitro and metastasis in vivo, is unknown. The studies ….demonstrate that AMF is the previously cloned cytokine and enzyme designated as neuroleukin, and phosphohexose isomerase (PHI), which has been independently implicated in cell motility, and to be a cancer progression marker.
Specific PHI inhibitors (carbohydrate phosphates) inhibited enzymatic activity and AMF-induced cell motility."

6. Verma, P C, et al. Study of serum phosphohexose isomerase (PHI) levels in the management of head and neck malignancies. *Indian J Otolaryngol Head Neck Surg*. 2001 Jan; 53(1):40-6. http://www.ncbi.nlm.nih.gov/pubmed/23119750

   "Study showed that estimation of serum PHI levels have significant role in diagnosis of cancer, early detection of residual growth, recurrent growth and secondaries"

7. Niizeki H, Kobayashi M, et al. Hypoxia enhances the expression of AMF and the motility of human pancreatic cancer cells. *Br J Cancer*. 2002 Jun 17; 86(12):1914-1919. http://www.ncbi.nlm.nih.gov/pubmed/12085186

   "The incidence of distant metastases is higher in the tumors with low oxygen pressure than in those with high oxygen pressure"

8. Takanami, I., et al. Autocrine motility factor receptor gene expression and cell motility in lung cancer cell lines. *Oncol Rep* 2002 Jan-Feb; 9(1): 125-128. http://www.ncbi.nlm.nih.gov/pubmed/11748469

   "We conclude that the presence of higher AMF-R gene expression and tumor cell motility via receptor in response to the stimulation of AMF could be an important aspect in the invasion and metastasis of lung cancer cell lines"

9. Tsutsumi, S, et al. Overexpression of the AMF/P-G-Isomerase Induces Transformation and Survival of NIH-3T3 Fibroblasts. *Cancer Res* 2003 Jan 1; 63(1):242-249. http://cancerres.aacrjournals.org/content/63/1/242.abstract

   "AMF/PGI is a ubiquitous cytosolic enzyme and is produced as a leaderless secretory protein, released from cells via a non-classical pathway. Increased expression of AMF/PGI and its receptor/CXXC-R has been found in a wide spectrum of malignancies, and is associated with cancer progression and metastasis….Ectopic overexpression of AMF/PGI results in its secretion and activation via a constitutive autocrine activation loop that renders the cells highly motile, acquiring a transformed phenotype *in vitro and* tumorigenicity *in vivo."*

10. Yanagawa T, et al., Novel roles of the autocrine motility factor/phosphoglucose isomerase (PGI or PHI) in tumor malignancy. *Endocr Relat Cancer*. 2004 Dec; 11(4):749-759. – 99 References. http://erc.endocrinology-journals.org/content/11/4/749.full

    "The enzyme is a regulatory catalyst of anaerobic Embden-Meyerhof glycolitic and glucogenetic pathways by reversibly converting G-6-P to F-6-P. It is the human AMF. As such, it stimulates cell motility in an autocrine manner and closely related to malignancy. It is a cytokine of the neurokine family"

11. Jiang, W G, et al. Expression of autocrine motility factor (AMF) and its receptor AMFR, in human breast cancer. *Journal of Histochemestry & Cytochemistry* 2006; 54(2):231-241. http://jhc.sagepub.com/content/54/2/231.full.pdf

    "AMF and AMFR are overexpressed in human breast cancer and are negatively associated with patients' clinical outcome. This strongly indicates that the AMF–AMFR complex plays an important role in the progression of breast cancer, as well as having a prognostic role"

12. Dobashi, Y, et al. Differential expression and pathological significance of AMF/G-6-phosphate isomerase expression in human lung carcinomas. *J Pathol* 2006 Dec; 210(4): 431-440. http://www.ncbi.nlm.nih.gov/pubmed/17029220

"AMF was detected in a major proportion of lung carcinomas, and may play a part not only in proliferation and/or progression of the tumors, but also, possibly, in the differentiation of SCLC. Furthermore, higher mRNA expression may be related to the high metastatic potential in NSCLC."
"AMF promoted cell motility in autocrine pathways, but was later shown to have a function as a mitogen."

13. Funasaka T, Raz A. The role of autocrine motility factor in tumor and tumor microenvironment. *Cancer Metastasis Rev.* Tumor Progression and Metastasis Program, Barbara Ann Karmanos Cancer Institute 2007 Dec; 26(3-4):725-35. http://www.ncbi.nlm.nih.gov/pubmed/17828376

"AMF is a multifunctional protein capable of affecting cell migration, invasion, proliferation, and survival, and possesses phosphoglucose isomerase activity and can catalyze the step in glycolysis and gluconeogenesis"

14. Schandl, E K. The cancer profile and its clinical applications, *Townsend Letter*, 2010 August/September; pages 84-86. http://townsendletter.com/AugSept2010/cancerprofile0810.html

"Elevated plasma levels may lead to metastatic events: cytokinetic vibration and dislodgement of the cancerous cell from its neighboring environment and consequent embolism via lymph or blood flow to distant sites"

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of April 1, 2013]
[CITE: 21CFR862.1570]

See Related Information[22]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

PART 862 -- CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES

Subpart B--Clinical Chemistry Test Systems

Sec. 862.1570 Phosphohexose isomerase test system.

(a) *Identification.* A phosphohexose isomerase test system is a device intended to measure the activity of the enzyme phosphohexose isomerase in serum. Measurements of phosphohexose isomerase are used

in the diagnosis and treatment of muscle diseases such as muscular dystrophy, liver diseases such as hepatitis or cirrhosis, and metastatic carcinoma.

(b) *Classification.* Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to 862.9.

[52 FR 16122, May 1, 1987, as amended at 65 FR 2307, Jan. 14, 2000]

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of April 1, 2013]
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See Related Information[22]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

PART 862 -- CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES

Subpart B--Clinical Chemistry Test Systems

Sec. 862.1155 Human chorionic gonadotropin (HCG) test system.

(a) *Human chorionic gonadotropin (HCG) test system intended for the early detection of pregnancy* -- (1) *Identification.* A human chorionic gonadotropin (HCG) test system is a device intended for the early detection of pregnancy is intended to measure HCG, a placental hormone, in plasma or urine.

(2) *Classification.* Class II.

(b) *Human chorionic gonadotropin (HCG) test system intended for any uses other than early detection of pregnancy* --(1) *Identification.* A human chorionic gonadotropin (HCG) test system is a device intended for any uses other than early detection of pregnancy (such as an aid in the diagnosis, prognosis, and management of treatment of persons with certain tumors or carcinomas) is intended to measure HCG, a placental hormone, in plasma or urine.

(2) *Classification.* Class III.

(3) *Date PMA or notice of completion of a PDP is required.* As of the enactment date of the amendments, May 28, 1976, an approval under section 515 of the act is required before the device described in paragraph (b)(1) may be commercially distributed. See 862.3.

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