

1890  
1990  
KARGER

Vol. 11, 1990

# Tumor Biology

**The Journal of the International Society for  
Oncodevelopmental Biology and Medicine (ISOBM)**

Founded 1980 as 'Oncodevelopmental Biology and Medicine' by the ISOBM  
(editors W.H. Fishman and H. Hirai), continued as 'Tumour Biology'  
(editors H. Hirai and A.M. Neville) 1984-1986

**Editors-in-Chief**

H. Hirai, Tokyo  
A.M. Neville, Zürich

**Managing Editor**

A. Malkin, Toronto

**Associate Editors**

E. Alpert, Montreal  
S. von Kleist, Freiburg i.Br.  
E.A. Nunez, Paris  
M. Seppälä, Helsinki  
A. Yachi, Sapporo

**Editorial Board**

G.I. Abelev, Moscow  
R.W. Baldwin, Nottingham  
L. Bélanger, Quebec  
J. Breborowicz, Poznan  
P. Burtin, Villejuif  
T.M. Chu, Buffalo, N.Y.  
Y. Endo, Tokyo  
W.H. Fishman, La Jolla, Calif.  
H.A. Fritsche, Houston, Tex.  
D.M. Goldenberg, Newark, N.J.  
K.M. Grigor, Edinburgh  
S. Hammarström, Stockholm  
P.J. Higgins, Albany, N.Y.  
C.H.W. Horne, Newcastle upon Tyne  
K. Imai, Sapporo  
R. Lamerz, München  
F.L. Lorscheider, Calgary  
J.-P. Mach, Lausanne  
J. Masopust, Prague  
R.F. Masseyeff, Nice  
S. Nishi, Sapporo  
B. Nørgaard-Pedersen, Copenhagen  
M.K. Schwartz, New York, N.Y.  
S. Sell, Houston, Tex.  
H.J. Staab, München  
K. Taketa, Takamatsu  
A. Talerman, Chicago, Ill.  
Y.S. Tatarinov, Moscow  
Y. Tsuchida, Tokyo  
J. Uriel, Villejuif  
B. Wahren, Stockholm  
S. Yachnin, Chicago, Ill.

**KARGER**

## Contents Vol. 11, 1990

No. 1-2	<b>Editorial</b>	
	Recent Developments concerning the Carcinoembryonic Antigen Gene Family and Their Clinical Implications. Report on the XVIIth Meeting of the International Society for Oncodevelopmental Biology and Medicine, Freiburg, FRG (September 18-22, 1989)	1
	Zimmermann, W.; Thompson, J. . . . .	
	<b>Original Papers</b>	
	Tumor Specificity of Monoclonal Antibodies to Carcinoembryonic Antigen. Immunohistochemical Analysis (With 2 color plates)	
	Zoubir, F.; Zeromski, J.; Sikora, J.; Szmeja, J.; Hedin, A.; Hammarström, S. . . . .	5
	Characterization of Monoclonal Antibodies Reactive with Normal Resting, Lactating and Neoplastic Human Breast	
	Skilton, R.A.; Earl, H.M.; Gore, M.E.; McIlhinney, R.A.J.; Gusterson, B.A.; Wilson, P.; Coombes, R.C.; Neville, A.M. . . . .	20
	Serine Proteinase Inhibitors Produced by Human Melanoma Cell Lines	
	Giacomoni, D.; Najmabadi, F.; Dray, S. . . . .	39
	Mechanism of Clearance of Circulating CA19-9 in Rats	
	Adachi, M.; Sekine, T.; Umemoto, A.; Tsukikawa, S.; Imai, K.; Yachi, A. . . . .	51
	<b>XVIIth Meeting of the International Society for Oncodevelopmental Biology and Medicine</b>	
	Freiburg (FRG), September 18-22, 1989	
	Workshop Report: Proposed Nomenclature for the Carcinoembryonic Antigen (CEA) Gene Family	
	Barnett, T.; Zimmermann, W. . . . .	59
	Abstracts Presented by Members of the ISOBM . . . . .	64
No. 3	<b>Original Papers</b>	
	Protein Factor of Fertility in Malignancies	
	Tatarinov, Y.S.; Shcherbakova, L.A.; Olefirenko, G.A.; Petrunin, D.D. . . . .	113
	Comparative Analysis of the Reduction of Oxaloacetate by Human Hepatoma and Normal Liver Extracts	
	Mazo, A.; Forner, A.; Domènech, C.; Busquets, M.; Gelpí, J.L.I.; Cortés, A. . . . .	120
	Dietary Milk Proteins Inhibit the Development of Dimethylhydrazine-Induced Malignancy	
	Papenburg, R.; Bounous, G.; Fleiszer, D.; Gold, P. . . . .	129

---

Oncoprecipitins from Marine Invertebrates Are Glycoproteins with a Higher Specificity to Carcinoembryonic Antigen	137
Pavlenko, A.F.; Kurika, A.V.; Chicalovets, I.V.; Ovodov, Y.S. . . . .	137
Enhanced Expression and Secretion of an Epithelial Membrane Antigen (MA5) in a Human Mucinous Breast Tumor Line (BT549)	145
Williams, C.J.; Major, P.P.; Dion, A.S. . . . .	145
Radio-Immunolocalization in Nude Mice Using Anticytokeratin Monoclonal Antibodies (With 1 color plate)	158
Sundström, B.; Johansson, B.; Hietala, S.-O.; Stigbrand, T. . . . .	158
Individualization of the Cutoff Value for Serum Squamous-Cell Carcinoma Antigen Using a Sensitive Enzyme Immunoassay	167
Takeshima, N.; Nakamura, K.; Takeda, O.; Morioka, H.; Tamura, H.; Takasugi, N.; Kato, H. . . . .	167
<b>No. 4</b>	<b>Review</b>
In situ Hybridization: Application to the Study of Gene Expression during Experimental Hepatocarcinogenesis and Human Hepatocellular Carcinoma	173
Bernauau, D.; Feldmann, G. . . . .	173
<b>Original Papers</b>	
Immunohistochemical Analysis of Human Adenocarcinomas of the Lung Using the Monoclonal Antibody 44-3A6	181
Radosevich, J.A.; Noguchi, M.; Rosen, S.T.; Shimosato, Y. . . . .	181
Pre-Operative Tumour Marker Levels in Patients with Breast Cancer and Their Prognosis	189
van Dalen, A. . . . .	189
Mast Cell Kinetics during Tumor Growth	196
Lauria de Cidre, L.; Sacerdote de Lustig, E. . . . .	196
Increase of Epidermal Growth Factor Receptor Expression Associated with a Lack of Antiproliferative Effect of IFN- $\beta$ in Human Lung Cancer Nodules in Organotypic Culture	202
Martyré, M.-C.; Grimaux, M.; Beaupain, R. . . . .	202
Activity of Glycolytic Enzymes and Glucose-6-Phosphate Dehydrogenase in Smooth Muscle Proliferation	210
Elbers, J.R.J.; Rijken, G.; Staal, G.E.J.; van Unnik, J.A.M.; Roholl, P.J.M.; van Oirschot, B.A.; Oosting, J. . . . .	210
<i>Datura stramonium</i> Agglutinin-Reactive $\alpha$ -Fetoprotein Isoforms in Hepatocellular Carcinoma and Other Tumors	229
Taketa, K.; Ichikawa, E.; Yamamoto, T.; Kato, H.; Matsuura, S.; Taga, H.; Hirai, H. . . . .	229
<b>No. 5</b>	<b>Review</b>
The Epidermal Growth Factor. A Review of Structural and Functional Relationships in the Normal Organism and in Cancer Cells	229
Laurence, D.J.R.; Gusterson, B.A. . . . .	229
<b>Original Papers</b>	
Activity of Glycolytic Enzymes and Glucose-6-Phosphate Dehydrogenase in Lipoblastic and Neurogenic Proliferations	262
Elbers, J.R.J.; van Unnik, J.A.M.; Rijken, G.; Roholl, P.J.M.; van Oirschot, B.A.; Staal, G.E.J. . . . .	262

---

Monoclonal Antibodies Reactive with the Breast Carcinoma-Associated Mucin Core Protein Repeat Sequence Peptide Also Recognise the Ovarian Carcinoma-Associated Sebaceous Gland Antigen	274
Layton, G.T.; Devine, P.L.; Warren, J.A.; Birrell, G.; Xing, P.-X.; Ward, B.G.; McKenzie, I.F.C.	
<b>Letter to the Editor</b>	
Working Group on Tumor Marker Criteria (WGTMC)	
Bonfrer, J.M.G.	287
<b>No. 6      Original Papers</b>	
Clinical Usefulness of Prostate-Specific Antigen and Prostatic Acid Phosphatase in Patients with Prostatic Cancer	
Filella, X.; Molina, R.; Jo, J.; Umbert, B.; Bedini, J.L.; Ballesta, A.M.	289
Effect of Rat Developmental Stage at Initiation on the Expression of Biochemical Markers during Liver Tumor Promotion	
Decloitre, F.; Lafarge-Frayssinet, C.; Barroso, M.; Lechner, M.C.; Ouldelhkim, M.; Frayssinet, C.	295
Carcinoembryonic Antigen, Its Spatial Structure and Localization of Antigenic Determinants	
Pavlenko, A.F.; Chikalovets, I.V.; Kurika, A.V.; Glasunov, V.P.; Mikhalyuk, L.V.; Ovodov, Y.S.	306
Measurement of Immunoreactive Prothrombin Precursor and Vitamin-K-Dependent Gamma-Carboxylation in Human Hepatocellular Carcinoma Tissues: Decreased Carboxylation of Prothrombin Precursor as a Cause of Des-Gamma-Carboxyprothrombin Synthesis	
Ono, M.; Ohta, H.; Ohhira, M.; Sekiya, C.; Namiki, M.	319
Spontaneously Metastasizing Variants of a Human Lung Carcinoma Cell Line: Monoclonal Antibody Characterization	
Varki, N.M.; Estes, L.A.; Tseng, A.; Vu, T.P.	327
Acknowledgement to the Reviewers	339
Author Index	340
Subject Index	341

---

**Suppl. 1      Genetic Markers of Haematological Malignancy**  
Guest Editors: P.H. Pinkerton; M.D. Reis

# XVIIth Meeting of the International Society for Oncodevelopmental Biology and Medicine

Freiburg, September 18–22, 1989

Tumor Biol 1990;11:59–63

© 1990 S. Karger AG, Basel  
1010–4283/90/0112–0059\$2.75/0

## Workshop Report: Proposed Nomenclature for the Carcinoembryonic Antigen (CEA) Gene Family

T. Barnett<sup>a</sup>, W. Zimmermann<sup>b</sup>

<sup>a</sup>Miles Research Center, West Haven, Conn., USA;

<sup>b</sup>Institut für Immunbiologie, Universität Freiburg, BRD

A 'CEA' workshop was held recently during the XVIIth ISOBM Meeting in Freiburg, September 18–22, 1989. A major purpose of the workshop was to propose a systematic nomenclature to be used by all interested participants in describing members of the CEA and pregnancy-specific  $\beta_1$ -glycoprotein (PSG) or Schwangerschaftsprotein 1 (SP1) gene and protein families. The following proposal which found general agreement from participants is offered for adoption by those working in the field. By way of introducing new names for previously described genes, we have included an appendix that lists both the new and the old designations for CEA and PSG family members. Inquiries and inconsistencies related to this proposal should be addressed to one of the authors.

### CEA Gene and Protein Families

The CEA gene family (and the corresponding CEA protein family) are divided into the CEA and PSG subgroups based on

sequences similarities. Gene members are named with a three-letter designation following conventions of the Human Gene Mapping Workshop 9.5 and applied genetic conventions. The names of newly characterized protein members should include their apparent molecular weight. All nonhuman CEA-like genes should be abbreviated CGM (for CEA gene-family member) preceded by a genus and species prefix, e.g. mmCGM for *Mus musculus* CGM.

#### *CEA Subgroup*

The genes encoding well-characterized proteins are named according to protein names, e.g. the CEA gene encodes the 180-kD CEA polypeptide, the NCA gene encodes both the 50- and 90-kD NCA polypeptide forms and the BGP (not BGP1 gene) gene encodes BGP1 protein(s). All other members of the CEA subgroup are given provisional assignments by the investigator of CGM<sub>n</sub>, where n represents a previously unused number. For example, the recently described cDNA clone which probably corresponds to the NCA95 protein is named CGM6.

### PSG Subgroup

As for the CEA subgroup, PSG subgroup members will be designated PSGn. In order to avoid confusion, it was suggested that anyone who identifies a new member of this gene family can obtain a provisional number from one of the authors (W. Zimmermann). Where applicable, permanent assignments will be made at proposed annual CEA Workshops or as an ongoing process by the authors.

### mRNA Variants

RNA variants or polyadenylation variants of CEA or PSG gene family members, as determined by cDNA cloning, or provisionally on the basis of exon structure from genomic DNA, will be designated by the addition of lower-case letters. For example, CEAa and CEAb represent polyadenylation variants of the single CEA genomic transcription unit, while BGPa, BG Pb, BG P c and BG P d represent the alternate splice products of the BGP genomic transcription unit, and likewise describe the proteins they encode; newly discovered variants will be named in alphabetical sequence.

### Domains

The derived polypeptide sequences of the CEA family members can be subdivided by sequence comparison into several regions which are supposed to represent domains or signal sequences. They can be characterized as containing:

- (a) A *leader* [L] sequence (not domain).
- (b) An IgV-like or *N*-terminal [N] domain.

(c) IgC-like domains, comprising two different types designated A or B; the three repeating regions in CEA would be symbolized A1-B1, A2-B2, A3-B3, or most PSGs would show an A1-A2-B2 arrangement of IgC-like domains.

(d) Carboxy-terminal domains that are abbreviated as (i) M (for membrane-associated sequence) for those CEA family members with a hydrophobic domain that is likely cleaved for phosphatidylinositol glycan (PIG) linkage to membranes, such as is found in CEA, NCA and CGM6 precursor proteins; (ii) C for carboxy-terminal domains such as are found in PSG proteins that do not have the characteristics of PIG-tailed sequences (designated C, for C-terminal sequence); (iii) TM for domains that have hydrophobic qualities that are likely to be *transmembrane*, and (iv) Cyt for carboxy-terminal domains that are likely to be *cytoplasmatic*, such as those found in BGP isoforms (e.g. Cyt1 and Cyt2, for the sequence of BGPa and BG P c, respectively).

Examples: The CEA precursor protein would have the linear domain sequence L-N-A1-B1-A2-B2-A3-B3-M, the BGP isoform BGPa L-N-A1-B1-A2-TM-Cyt1 and PSG1a L-N-A1-A2-B2-Ca.

### Exons

Exons in genomic DNA are designated according to the regions or domains they contain; thus, the first exon of NCA, containing the 5' untranslated region of the mRNA (5'UTR) and some of the leader sequence, would be 5'/L, and the second exon, containing the remainder of the leader sequence and the N-terminal domain would be designated L/N, etc.

**Table 1.** CEA and PSG gene family members

Old gene or clone name	New gene or RNA name	Old gene or clone name	New gene or RNA name
<i>CEA subgroup</i>			<i>PSG subgroup</i>
CEA [1–4]	CEAa <sup>1</sup>	PSG93 [16], PS $\beta$ G-D [17], hPSP11 [18],	
CEA [5]	CEAb <sup>2</sup>	FL-NCA-2 [19], hPS3 [20],	
NCA [4, 6–9]	NCA	PSG1 <sub>a</sub> [21]	PSG1a
hsCGM6 [10], GN-1 [11], M6 [12]	CGM6	PSG16 [16]	PSG1b
BGPI [13], TM-1 CEA [14]	BGPa	PS $\beta$ G-C [17]	PSG1c
TM-2 CEA [14]	BGPb	FL-NCA-1 [22], PSG1 <sub>d</sub> [21]	PSG1d
TM-3 CEA [14]	BGPc	PS $\beta$ G-E [17]	PSG2
TM-4 CEA [14]	BGPd	pSP1-i [23], hc17 [24], PS35 [25]	PSG3
hsCGM1 [15]	CGM1	hsCGM4 [15], hHSP2 [18], PSG4 [21]	PSG4
hsCGM2 <sup>3</sup> [15]	CGM2	FL-NCA-3 [19], PS $\beta$ G HL [26]	PSG5
		hsCGM3 [15], PSG6 [21]	PSG6
		PSG7 [27]	PSG7
		CGM35 [5]	PSG8
		PS <sub>K<math>\alpha</math></sub> [28, 29]	PSG9
		PSG10 [29]	PSG10
		PS34 [25]	PSG11

<sup>1</sup> Short polyadenylation mRNA variant.<sup>2</sup> Long polyadenylation mRNA variant.<sup>3</sup> Although it was originally thought that this gene represents a separate entity more detailed evolutionary analyses indicate inclusion within the CEA subgroup [30].

A list of CEA and PSG gene family members, whose assignments are based on the conventions proposed above is presented in table 1.

## References

- Oikawa S, Nakazato H, Kosaki G: Primary structure of human carcinoembryonic antigen (CEA) deduced from cDNA sequence. *Biochem Biophys Res Commun* 1987;142:511–518.
- Zimmermann W, Ortlieb B, Friedrich R, et al: Isolation and characterization of cDNA clones encoding the human carcinoembryonic antigen reveal a highly conserved repeating structure. *Proc Natl Acad Sci USA* 1987;84:2960–2964.
- Beauchemin N, Benchimol S, Cournoyer D, et al: Isolation and characterization of full-length functional cDNA clones for human carcinoembryonic antigen. *Mol Cell Biol* 1987;7:3221–3230.
- Barnett T, Goebel SJ, Nothdurft MA, et al: Carcinoembryonic antigen family: Characterization of cDNAs coding for NCA and CEA and suggestion of nonrandom sequence variation in their conserved loop-domains. *Genomics* 1988;3:59–66.

5 Oikawa S, Inuzuka C, Kosaki G, et al: Exon-intron organization of a gene for pregnancy-specific  $\beta_1$ -glycoprotein, a subfamily member of CEA-family: implications for its characteristic repetitive domains and N-terminal sequences. *Biochem Biophys Res Commun* 1988;156:68-77.

6 Thompson JA, Pande H, Paxton RJ, et al: Molecular cloning of a gene belonging to the carcinoembryonic antigen gene family and discussion of a domain model. *Proc Natl Acad Sci USA* 1987;84: 2965-2969.

7 Oikawa S, Kosaki G, Nakazato H: Molecular cloning of a gene for a member of carcinoembryonic antigen (CEA) gene family; signal peptide and N-terminal domain sequences of nonspecific cross-reacting antigen (NCA). *Biochem Biophys Res Commun* 1987;146:464-469.

8 Neumaier M, Zimmermann W, Shively L, et al: Characterization of a cDNA clone for the nonspecific crossreacting antigen (NCA) and a comparison of NCA and carcinoembryonic antigen (CEA). *J Biol Chem* 1988;263:3202-3207.

9 Tawaragi Y, Oikawa S, Matsuoka Y, et al: Primary structure of nonspecific crossreacting antigen (NCA), a member of carcinoembryonic antigen (CEA) gene family, deduced from cDNA sequence. *Biochem Biophys Res Commun* 1988; 150:89-96.

10 Berling B, Zimmermann W, Thompson J: Identification of a new member of the CEA gene family expressed in the spleen of a patient suffering from chronic myeloid leukaemia (CML). XVIIth Meet Int Soc Oncodevelopmental Biology and Medicine, Freiburg 1989, p 52.

11 Matsuoka Y, Arakawa F, Kuroki M, et al: Cloning of cDNA encoding nonspecific cross-reacting antigen (NCA) of human normal granulocytes. XVIIth Meet Int Soc Oncodevelopmental Biology and Medicine, Freiburg 1989, p 53.

12 Boucher D, Cournoyer D, Fuks A, et al: Molecular cloning of cDNA clones corresponding to a new CEA member expressed in leukocytes. XVIIth Meet Int Soc Oncodevelopmental Biology and Medicine, Freiburg, 1989, p 53.

13 Hinoda Y, Neumaier M, Hefta SA, et al: Molecular cloning of a cDNA coding biliary glycoprotein I: primary structure of a glycoprotein immunologically crossreactive with carcinoembryonic antigen. *Proc Natl Acad Sci USA* 1988;85:6959-6963; correction: *Proc Natl Acad Sci USA* 1989;86:1668.

14 Barnett TR, Kretschmer A, Austen DA, et al: Carcinoembryonic antigens: Alternative splicing accounts for the multiple mRNAs that code for novel members of the carcinoembryonic antigen family. *J Cell Biol* 1989;108:267-276.

15 Thompson JA, Mauch E-M, Chen F-S, et al: Analysis of the size of the carcinoembryonic antigen (CEA) gene family: isolation and sequencing of N-terminal domain exons. *Biochem Biophys Res Commun* 1989;158:996-1004.

16 Watanabe S, Chou JY: Isolation and characterization of complementary DNAs encoding human pregnancy-specific  $\beta_1$ -glycoprotein. *J Biol Chem* 1988;263:2049-2054.

17 Streydio C, Lacka K, Swillens S, et al: The human pregnancy-specific  $\beta_1$ -glycoprotein (PS $\beta$ G) and the carcinoembryonic antigen (CEA)-related proteins are members of the same multigene family. *Biochem Biophys Res Commun* 1988;154:130-137.

18 Chan W-Y, Borjigin J, Zheng Q-X, et al: Characterization of cDNA encoding human pregnancy-specific  $\beta_1$ -glycoprotein from placenta and extra-placental tissues and their comparison with carcinoembryonic antigen. *DNA* 1988;7:545-555.

19 Khan WN, Hammarström S: Carcinoembryonic antigen gene family: molecular cloning of cDNA for a PS $\beta$ G/FL-NCA glycoprotein with a novel domain arrangement. *Biochem Biophys Res Commun* 1989;161:525-535.

20 Chan W-Y, Tease LA, Borjigin J, et al: Pregnancy specific  $\beta_1$ -glycoprotein mRNA is present in placental as well as in non-placental tissues. *Human Reprod* 1988;3:677-685.

21 Zimmermann W, Weiss M, Thompson JA: cDNA cloning demonstrates the expression of pregnancy-specific glycoprotein genes, a subgroup of the carcinoembryonic antigen gene family, in fetal liver. *Biochem Biophys Res Commun* 1989;163: 1197-1209.

22 Khan WN, Osterman A, Hammarström S: Molecular cloning and expression of cDNA for a carcinoembryonic antigen-related fetal liver glycoprotein. *Proc Natl Acad Sci USA* 1989;86:3332-3336.

23 Rooney BC, Horne CHW, Hardman N: Molecular cloning of a cDNA for human pregnancy-specific  $\beta_1$ -glycoprotein: homology with human carcinoembryonic antigen and related proteins. *Gene* 1988;71:439-449.

24 McLenaghan T, Mansfield B: Expression of CEA-related genes in the first trimester human placenta. *Biochem Biophys Res Commun* 1989;162: 1486-1493.

25 Arakawa F, Kuroki M, Misumi Y, et al: New members of cDNA clones belonging to pregnancy-specific  $\beta_1$ -glycoprotein (PS $\beta$ G). XVIIth Meet Int Soc Oncodevelopmental Biology and Medicine, Freiburg, 1989, p 58.

26 Oikawa S, Inuzuka C, Kuroki M, et al: A pregnancy-specific  $\beta_1$ -glycoprotein, a CEA family member, expressed in a human promyelocytic leukemia cell line, HL-60: structures of protein, mRNA and gene. *Biochem Biophys Res Commun* 1989; 163:1021-1031.

27 Thompson J, Koumari R, Wagner K, et al: The human pregnancy-specific glycoprotein genes are closely linked on chromosome 19 and reveal co-ordinated expression in the placenta. Submitted.

28 Barnett TR, Pickle II W, Rae PMM, et al: Human pregnancy-specific  $\beta_1$ -glycoprotein are coded within chromosome 19. *Am J Hum Genet* 1989; 44:890-893.

29 Barnett TR, Pickle II W: Novel pregnancy-specific  $\beta_1$ -glycoprotein cDNAs from the acute myelogenous leukemia cell line KG-1. Submitted.

30 Rudert F, Zimmermann W, Thompson JA: Intra- and interspecies analyses of the carcinoembryonic antigen (CEA) gene family reveal independent evolution in primates and rodents. *J Mol Evol* 1989;29:126-134.

Accepted: October 24, 1989

T. Barnett  
Miles Research Center  
400 Morgan Lane  
West Haven, CT 06516 (USA)

W. Zimmermann  
Institute of Immunobiology  
University of Freiburg  
Stefan-Meier-Strasse 8  
D-7800 Freiburg (FRG)