

Dynamic Institutionalization of Research in the Field of Colorectal Tumour Markers

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Abstract

Institutionalization and internationalization of modern interdisciplinary research belong to the essential components of scientific communications. Our purpose was to analyze scientometrically the dynamic science institutionalization on colorectal tumour markers as reflected in four information portals. In June 2017, a retrospective problem-oriented, title-word based search was performed in *Web of Science Core Collection (WoS)*, *MEDLINE* and *BIOSIS Citation Index (BIOSIS)* of *Web of Knowledge* as well as in *Scopus* for 1987-2016. The following scientometric parameters were comparatively assessed: i) annual dynamics of publications; ii) scientific institutions; iii) scientific forums; iv) authors; v) journals; vi) languages of publications and vii) citations. There were 497 publications abstracted in *WoS*, 427 in *Scopus*, 370 in *BIOSIS*, and 368 in *MEDLINE*. The articles were published in 16 languages in 197 journals by scientists from 50 countries in *Scopus*, in 6 languages in 164 journals by authors from 47 countries in *WoS*, in 10 languages in 136 journals by researchers from 37 countries in *BIOSIS*, and in 14 languages in 178 journals in *MEDLINE*. The most influential scientific institutions were the University of Helsinki, University of Heidelberg, German Cancer Research Center, etc. The annual meetings of the American Association for Cancer Research, the American Gastroenterological Association (Digestive Disease Week) and the American Society of Clinical Oncology attracted the attention of most scientists from the world. The most productive authors were O. Topolcan, C.A.J. Haglund, M.J. Duffy, etc. The so-called 'core' journals containing most papers on this topic were *Anticancer Res*, *Br J Cancer*, *Cancer Res*, etc. The paper by R.C. Bast et al. (*J Clin Oncol* 2001; 19:1865-78) received 702 citations in *Scopus*, 575 in *WoS*, and 320 in *BIOSIS*. Our results along with this collection of comprehensive factual information are of interest for the coloproctologists from smaller countries, institutional and national science managers and journal editors.

Keywords: Colorectal Tumour Markers; Science Institutionalization; Scientometrics; Publication Output; Citation Activity

List of abbreviations: *BIOSIS* - *BIOSIS Citation Index*; *CA* - cancer antigen; *CEA* - carcinoembryonic antigen; *CRC* - colorectal cancer; *EGTM* - European Group on Tumor Markers; *WoS* - *Web of Science Core Collection*

Introduction

Colorectal cancer (CRC) is a common pathology of rising socio-medical importance worldwide. The CRC develops through at least three major pathways, including chromosomal instability, mismatch repair, and methylator phenotype [1]. Techniques to recognize CRC at the molecular level facilitate development of new signature drugs designed to inhibit the unique pathways of its growth and immunity. The CRC advances as a consequence of genomic instability characterized by various genetic and epigenetic alterations [2]. Its molecular heterogeneity explains the large variability in patient's prognosis and treatment response, emphasizing the need for development of accurate prognostic and predictive biomarkers thus guiding the effective clinical decision-making and treatment.

The American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology convene an Expert Panel in order to develop an evidence-based guideline to help establish standard molecular biomarker testing, guide targeted therapies, and advance personalized care for CRC patients [3]. A comprehensive literature search of more than 4000 articles gathers data to inform this guideline. Twenty-one guideline statements such as eight recommendations, 10 expert consensus opinions and three no recommendations have been established. Evidence supports mutational testing for genes in the anti-epidermal growth factor signaling pathway, since they provide clinically actionable information as negative predictors of benefit to anti-epidermal growth factor receptor monoclonal antibody therapies for targeted therapy of CRC. Mutations in several biomarkers present with clear prognostic value. Laboratory approaches to operationalize

molecular testing for predictive and prognostic molecular biomarkers involve selection of assays, type of specimens to be tested, timing of ordering of tests and turnaround time for testing results [3].

Serum expression levels of miR-17, miR-21, and miR-92 represent valuable markers for recurrence after adjuvant chemotherapy in colon cancer patients [4].

A systematic review of 156 studies dealing with the sensitivity, specificity, statistical heterogeneity and ability to predict CRC recurrence and metastases for three tumour markers for CRC and esophageal cancer such as carcinoembryonic antigen (CEA), cancer antigen (CA) 19-9 and CA125 demonstrates that CEA out-performs both CA19-9 and CA125 [5].

The results from literature search about the prognostic value of some systemic inflammation markers such neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio in relation to CRC outcomes prove that they can be used to predict the chemotherapeutic outcome and monitor tumour progression in patients with unresectable metastatic disease [6].

In the next future, there will be a complete panel of clinical biomarkers to use in every setting of CRC disease [7]. In addition, one will receive information about the prognostic significance of the expression of serum and tissue colorectal tumour marker and will be oriented in the choice of the adequate treatment of CRC patients.

Recently, the dynamics of the international scientific communications in the field of colorectal tumour markers as reflected in five information portals such as *Web of Science Core Collection (WOS)*, *MEDLINE*, *BIOSIS Citation Index (BIOSIS)*, *Derwent Innovations Index and Scopus* was comprehensively analyzed [8].

Scientometrics represents a branch of modern applied science of science examining the structure and dynamics of the scientific communications. Two decades ago, two original scientometric concepts about some substantial components of modern science were launched [9]. The first concept was devoted the unity of the publication output, abstracting of publications in secondary information sources and data-bases, and citations to these publications and explained the mutual relationships between these components of the scientific communications. The second concept analyzed the unity of the institutionalization, interdisciplinarity and internationalization of contemporary science and university education and elucidated the role of the integration of these components for further enhancement of research effectiveness and improvement of science infrastructure at individual, local, national and international level as well.

Problem-oriented scientometric investigations of these aspects of science and the international collaboration under the conditions of globalization and competition contribute to enhancement of the quality and prestige of science forefront in powerful and smaller countries as well [10,11]. Institutionalization of research includes the intrinsic features of historically established disciplinary organization of scientific and higher educational structures concordant with enhanced present requirements and already gained social recognition of the topic. Thus it is an essential component of the mature scientific discipline or subdiscipline [9,10].

Along with the acknowledged problem-oriented denominations of single institutions of different organizational type, the following essential components belong to science institutionalization [10]:

- the organization of national and international scientific forums on a concrete interdisciplinary (or narrow-monodisciplinary) topic;
- the regular publication of problem-oriented and narrow- or broad-profile inter- or monodisciplinary journals and monographs and their subsequent inclusion in secondary information sources and data-bases;
- foundation of national and international scientific societies and associations;
- establishing of corresponding university departments and/or their subdivisions performing a regular students' education;
- introduction of postgraduate studies and preparation of doctoral dissertations;
- introduction of the topic into university students' curricula, initially, in the form of extracurricular activity such as invited lectures delivered by experts from the same country and abroad, publication of textbooks and manuals, summer schools, etc.;
- creation and subsequent dynamic development of corresponding paradigms or paradigm circles, etc.

Our purpose is to analyze scientometrically the dynamic science institutionalization on colorectal tumour markers as reflected in four information portals and to outline the significant institutions, scientists, conference proceedings and journals in this rapidly advancing field.

Materials and Methods

In June 2017, a retrospective problem-oriented, title-word based search was performed in *Web of Science Core Collection (WoS)*, *MEDLINE* and *BIOSIS* of *Web of Knowledge* as well as in *Scopus* for 1987-2016. The following scientometric parameters of the publication output and citation activity were comparatively assessed: i) annual dynamics of publications - number of abstracted publications - total and per year; ii) scientific institutions - organizational types, country belonging, thematic belonging and international collaboration; iii) scientific forums - number of publications, country belonging, thematic belonging; iv) authors - number of unique names, number of publications, country belonging and international collaboration; v) journals - total and per year, number of abstracted articles from single journals, number of articles in own national and in foreign journals, number of

journals specialized in (bio)markers, vi) types of documents; vii) languages of publications - number of publications in a single journal, and viii) citations (number of citations to publications by single authors received in *WoS*, *BIOSIS* and *Scopus* during this 30-year period and computerized citation metrics).

Results

The comprehensive scientometric analysis by using a constellation of specific indicators for publication output and citation activity has resulted in the preparation of a series of non-Gaussian distributions.

Our results reveal several essential peculiarities of the dynamic structure of the publication and citation output on this topic during these three decades. They are systematized in ten tables and illustrated on five figures.

The general bibliometric characteristics of four data-bases can be seen in Table 1. The annual dynamics of the number of publications abstracted in four data-bases during this 30-year period on colorectal tumour markers is illustrated on Figure 1 through Figure 3.

Parameter	WoS	BIOSIS	MEDLINE	Scopus
Total number of publications	497	370	368	427
Total number of journals	164	136	178	197
Total number of journals with one article only	95	87	119	90
Percentage of these journals	57.93	63.97	66.85	45.69
Total number of journals with ≥10 articles each	10	6	4	3
Percentage of these journals	6.10	4.41	2.25	1.52
Total number of languages (n=16)	6	10	14	16
Total number of countries of authors (n=53)	47	50	N/A	37

Table 1: General bibliometric characteristics of four data-bases on this topic

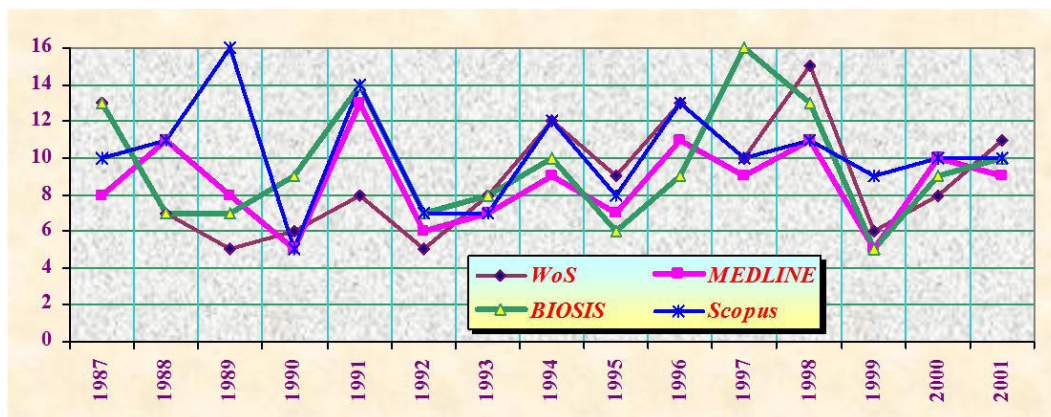


Figure 1: Annual dynamics (1987-2001) of the number of publications on the topic abstracted in four data-bases

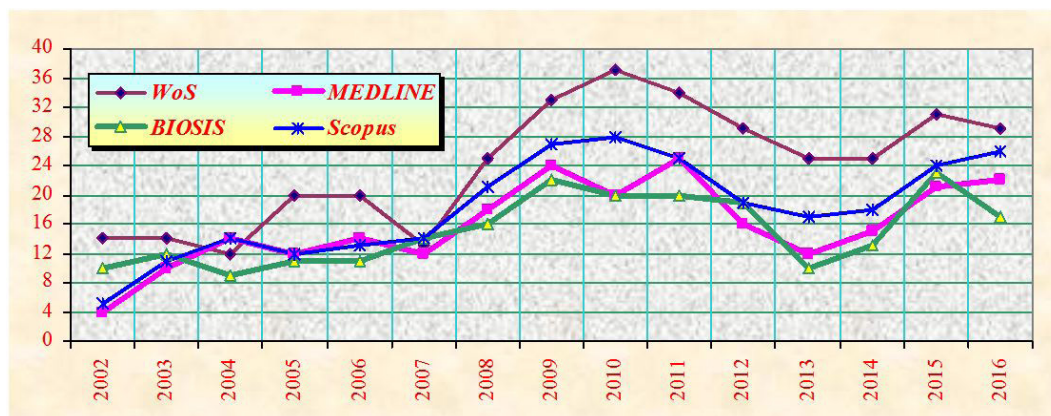


Figure 2: Annual dynamics (2002-2016) of the number of publications on the topic abstracted in four data-bases

It is a noteworthy fact that *WoS* presents with the highest rate of increase of the abstracted publications between the first five-year period (1987-1991) and the last one (2012-2016) - of 71,94%.

The country distribution according to the number of publications in *WoS*, *BIOSIS* and *Scopus* is demonstrated on Figure 4 while the language distribution of all the publications abstracted in four data-bases is shown on Figure 5.

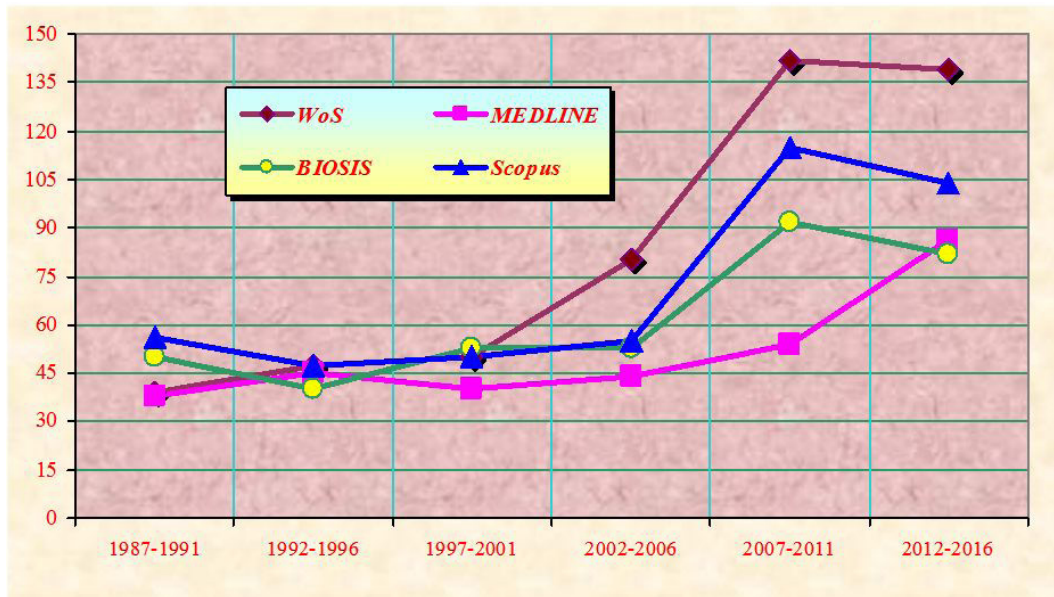


Figure 3: Cumulative five-year annual dynamics (1987-2016) of the number of publications on the topic abstracted in four data-bases

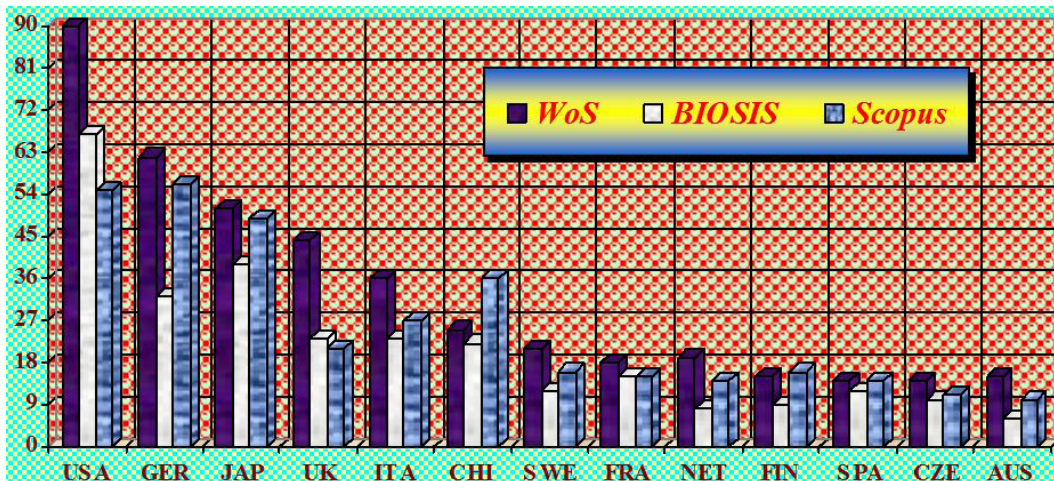


Figure 4: Country distribution according to the number of publications on the topic abstracted in three data-bases

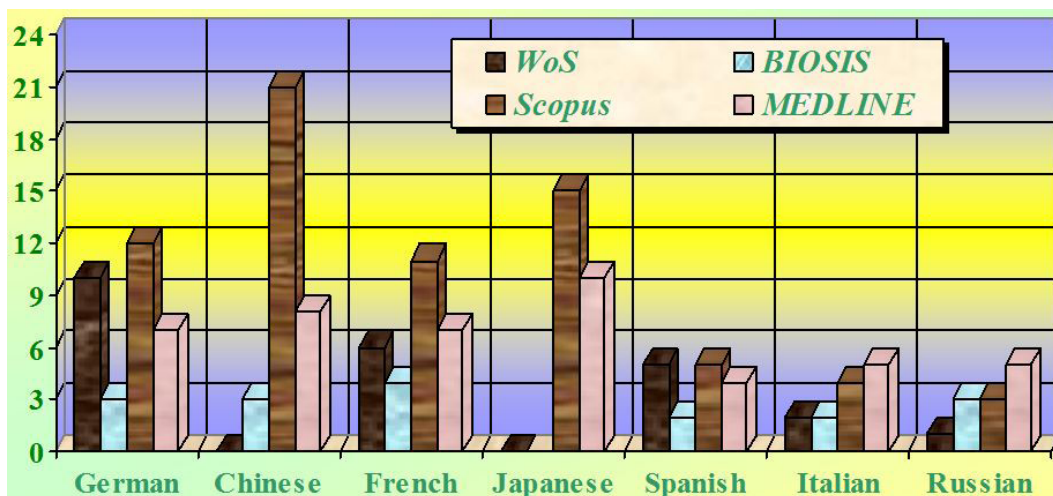


Figure 5: Language distribution of publications on the topic abstracted in four data-bases

The different types of documents of these publications are listed in Table 2. The journals containing most abstracted publications on this topic, the so-called ‘core’ journals, are comparatively indicated in Table 3 while the highly specialized, narrow-topic journals containing the term of ‘(bio)markers’ in their titles are listed in Table 4.

Document type	WoS		BIOSIS		MEDLINE		Scopus	
journal article	276	55.53	216	58.38	350	95.11	341	79.86
meeting abstract	174	35.01	145	39.19	-	-	-	-
review	15	3.02	-	-	32	8.70	38	8.90
congress proceedings	19	3.82	-	-	-	-	20	4.68
letter-to-the-editor	13	2.62	3	0.81	22	3.99	11	2.58
editorial	6	1.21	-	-	4	1.09	2	0.47
book chapter	1	0.20	6	0.54	-	-	2	0.47
evaluation study	-	-	-	-	-	-	10	2.72
multicentre study	-	-	-	-	-	-	5	1.36

Table 2: Document type distribution in four data-bases

Rank	Journal title	WoS	BIOSIS	MEDLINE	Scopus
1.	<i>Anticancer Res</i>	23	28	18	18
2.	<i>Gastroenterology</i>	23	23	1	1
3.	<i>Tumor Biol</i>	10	19	4	4
4.	<i>Br J Cancer</i>	18	14	12	13
5.	<i>Cancer Res</i>	21	14	8	8
6.	<i>J Clin Oncol</i>	28	3	11	6
7.	<i>Dis. Colon Rectum</i>	14	3	11	13
8.	<i>Int J Cancer</i>	9	9	9	9
9.	<i>Eur J Cancer</i>	10	15	3	3
10.	<i>Cancer</i>	8	7	8	8

Table 3: 'Core' journals on the topic in four data-bases

Rank	Journal title	WoS	MEDLINE	BIOSIS	Scopus
1.	<i>Int J Biol Markers</i>	1	6	3	6
2.	<i>Cancer Biomarkers</i>	2	2	2	3
3.	<i>J Tumor Marker Oncol</i>	-	-	4	1
4.	<i>Disease Markers</i>	1	1	-	1
5.	<i>Cancer Epidemiol Biomarkers Prev</i>	1	-	1	-
6.	<i>Meth Mol Med Tumor Marker Protocol</i>	-	-	2	-
7.	<i>Genomic Med Biomarkers Health Sci</i>	-	-	-	1

Table 4: Specialized journals with the term of '(bio) markers' in their titles in four data-bases

Some essential aspects of science institutionalization concerning the scientific forums in WoS and BIOSIS are systematized in Table 5 and Table 6.

Parameter	WoS	BIOSIS
<i>number of forum titles</i>	45	49
<i>number of unique forums</i>	63	91
<i>number of publications</i>	116	144
<i>number of forums with a single event only</i>	37	37
<i>maximal number of events of a unique forum</i>	6	20
<i>maximal number of publications in a unique forum</i>	13	33
<i>Genomic Med Biomarkers Health Sci</i>	-	-

Table 5: Bibliometric characteristics of scientific forums on the topic in WoS and BIOSIS

The following scientific meetings with the term of tumour markers in their nominations contain publications devoted to colorectal tumour markers:

First International Conference on Trace Elements, Free Radicals, Tumour Markers, Chromosomal Analysis, and Cytokines in Clinical Medicine and Biochemistry held in Kuwait, on March 20-23, 1995.

9th, 11th, 13th and 15th International Symposium on Tumor Markers held in Hamburg, Germany, with a total of 6 publications on this topic.

Scientific forum title	WoS		BIOSIS	
	events	papers	events	papers
Annual Meeting of the American Association for Cancer Research	4	8	20	33
Digestive Disease Week	6	10	11	19
Annual Meeting of the US and Canadian Academy of Pathology	6	9	7	9
European Society for Medical Oncology Congress	4	5	2	2
Annual Meeting of the American Society of Clinical Oncology	5	13	-	-
Meeting of the International Society for Oncodevelopmental Biology and Medicine	1	1	6	10

Table 6: Scientific forums with most events and papers in them on the topic in WoS and BIOSIS

13th International Conference on Human Tumor Markers held in Singapore on June 16-19, 1996.

AACC Regulatory-Affairs-Committee Tumor Marker Conference held in Washington, DC, USA, on March 12, 1997.

The most productive institutions on the topic in WoS and Scopus are presented in Table 7.

Rank	Institution	Country	WoS	Scopus
1.	University of Helsinki	Finland	17	18
2.	Universität Heidelberg	Germany	12	11
3.	German Cancer Research Center	Germany	11	10
4.	Uppsala University	Sweden	12	9
5.	Harvard University	USA	13	8
6.	Ludwig-Maximilians-Universität München	Germany	9	12
7.	Mayo Clinic	USA	14	6
8.	Humboldt Universität Berlin	Germany	11	8
9.	Chang Gung University	Taiwan (R.O.C.)	10	6
10.	Charles University of Prague	Czech Republic	9	6

Table 7: Most productive institutions on the topic in WoS and in Scopus

The following scientific institutions contain the term of 'tumour marker' in their nominations:

Institute of Tumor Marker Oncology, NL-2801 Gouda, the Netherlands

University of Pittsburgh School of Medicine, Pittsburgh Cancer Institute, Tumor Marker Laboratory, Pittsburgh, PA 15261, USA

ZeTDT GmbH, Center of Clinical and Experimental Tumor Marker Diagnosis and Therapy, D-20095 Hamburg, Germany

Chinese Academy of Medical Sciences, Cancer Institute and Hospital, Tumor Marker Research Center, Beijing, Republic of China

Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Department of Tumor Markers, 02-781 Warsaw, Poland

Al-Azhar University, Tumor Marker Oncology Research Center, Cairo, Egypt

The University of Texas MD Anderson Cancer Center, ASCO, Tumor Marker Panel, Houston, TX 77030, USA

Montefiore Medical Center, The Albert Einstein College of Medicine, Department of Pathology, Tumor Marker Laboratory, Bronx, NY, USA

The most productive authors on the topic in WoS, MEDLINE and BIOSIS are displayed in Table 8 and their current addresses are listed below:

Michael J. Duffy; UCD Clinical Research Centre, St. Vincent's University Hospital, Dublin 4, Ireland; e-mail: michael.j.duffy@ucd.ie

Robert C. Bast, Jr; University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA; e-mail: rbast@mdanderson.org

Caj Haglund; Department of Surgery, Helsinki University Central Hospital, P.O. Box 340, 00029 Hus, Helsinki, Finland; e-mail: caj.haglund@hus.fi

Bengt Glimelius; Department of Immunology, Genetics and Pathology, Experimental and Clinical Oncology; Research Group Bengt Glimelius, Uppsala University, Uppsala, Sweden; e-mail: bengt.glimelius@igp.uu.se

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Lubos Holubec; Department of Clinical Oncology and Radiotherapy, Biomedical Center, Medical Faculty Hospital, 305 99 Plzen, Charles University, Czech Republic; e-mail: holubec@fnplzen.cz

Rank	Authors	Country	WoS	BIOSIS	MEDLINE
1.	CAJ Haglund	Finland	9	8	8
2.	O Topolcan	Czech Republic	7	7	6
3.	MJ Duffy	Ireland	9	3	6
4.	I Zlobec	Switzerland	7	5	3
5.	M Levy	Czech Republic	6	7	-
6.	L Lipska	Czech Republic	6	7	-
7.	B Glimelius	Sweden	7	-	6
8.	R Lamerz	Germany	5	4	3
9.	L Holubec	Czech Republic	7	3	-
10.	A Lugli	Switzerland	6	4	-

Table 8: Most productive authors on the topic in three data-bases

Prof. Robert C. Bast Jr. presents with 12 papers on tumour markers published between 1998 and 2017 and abstracted in WoS. The sum of times cited without self-citations is 2546 and the sum of citing articles without self-citations is 2281.

There is a highly productive research group, i. e. European Group on Tumor Markers (EGTM).

The ten most cited articles on the topic in WoS, BIOSIS and Scopus are demonstrated in Table 9.

First author's name	Journal title, volume, year & pages	WoS	BIOSIS	Scopus
RC Bast Jr et al.	J Clin Oncol 2001; 19: 1865-78	575	320	702
RC Bast Jr et al.	J Clin Oncol 1996; 14: 2843-77	388	233	489
B Fernandes et al.	Cancer Res 1991 51: 718-23	323	266	329
MJ Duffy et al.	Eur J Cancer 2007 43: 1348-60	262	165	296
CM Sturgeon et al.	Clin Chem 2008 54: E11-79	244	absent	288
MJ Duffy et al.	Eur J Cancer 2003 39: 718-27	220	126	260
TC Smyrk et al.	Cancer 2001 91: 2417-22	198	142	222
HL McLeod et al.	Br J Cancer 1999 79: 191-203	170	109	200
J Saarnio et al.	Am J Pathol 1998 153: 279-85	163	130	178
SL Carrithers et al.	Proc Natl Acad Sci USA 1996 93: 14827-32	144	115	151

Table 9: Ten most cited articles on the topic in three data-bases

Citation parameter	WoS	BIOSIS
total number of publications	497	370
sum of the times cited	8990	4570
sum of the times cited without self-citations	8796	4477
percentage of these times cited	97.84	97.96
citing articles	7690	4110
citing articles without self-citations	7586	4058
percentage of these citing articles	98.65	98.73
Average citations per item	18.09	12.35
Average citations per year	290.00	147.42
Articles cited at least once	299	203
percentage of these articles	60.16	54.86
H-index	48	35

Table 10: Cumulative citation patterns on the topic in WoS and BIOSIS

The results from the computerized citation metrics available in *WoS* and *BIOSIS* indicate the high international prestige of the topic of the colorectal tumour markers and convincingly prove the rising interest of the world scientific community (Table 10). The value of h-index is high, indeed [12].

Discussions

We establish well-known, typical stratification patterns concerning the publication output and citation activity at any levels of examination. The emergence of Finish science and Czech one on the international information market stresses, indeed. It is due to a favourable infrastructure, on the one hand, and to intensive and fruitful international collaboration, on the other hand, too.

Our results display the enormous capacities of the computer-aided scientometric approach to interdisciplinary science. The systematized files with bibliographic, abstracted and full-text information could successfully be used by experienced specialists and beginners as well as in practice-oriented research involving national and/or international collaborative teams.

In the spirit of traditional scientometric treatises, let us mention the modest contribution to this topic of Bulgarian medical science, too. A paper by our team has been abstracted in *BIOSIS* [13] and two other papers published in a Bulgarian surgical journal have been abstracted in *MEDLINE* [14,15].

It should be mentioned, however, that there are certain attractive advantages and considerable disadvantages of some of these databases extensively discussed elsewhere [16]. The different extent of relevant journals' coverage by single data-bases is related to their specific editorial policy. It is, however, of crucial importance for end users and scientometricians and deserves detailed comparative investigations. Further improvements of these editorial policies are needed to optimize the coverage scope of the primary literature and to refine the indexing algorithms of the corresponding information centres.

Some newly-published investigations testify to the uninterrupted interest in science institutionalization worldwide. A historical case study of the institutionalization of laboratory work in Japan from the 1880s to the 1930s is performed [17]. The professionalization and institutionalization of history of psychology as a specialty in the United States of America is analyzed from a historical-sociological model [18]. A socio-historical analysis of the institutionalization of multidisciplinary studies is carried out by examining the demand for and availability of program types in higher education and research institutions between 1950 and 1970 in France [19]. Although in the late XIX and early XX centuries German scholarship represents a model that deeply inspires sociologists across the United States, the institutionalization of sociology within American universities takes place much earlier and faster than in their German counterparts [20]. The institutionalization of diabetes mellitus research in obstructive sleep apnea patients is followed-up [21].

The analysis of a comprehensive historical database from 1900 to 2010 uncovers both stable and dynamic patterns of production and productivity in Germany, France, Belgium, and Luxembourg and shows the varying contributions of different organizational forms, especially research universities and research institutes [22]. Comparing the institutionalization pathways that create the conditions necessary for continuous and strong growth in scientific productivity identifies the research university as the key organizational form across countries.

Institutionalization framework elements such as nominal, leadership, administrative support, multi-year funding, research targets, formal researcher-to-researcher exchange, visibility, evaluation, and supporting characteristics are examined in five cases studies of institutionalization framework in order to explain the development of international university research ventures between US universities, on the one hand, and China and Singapore, on the other hand [23].

A systematic bibliographic analysis of research papers published in three most prominent journals in the field of science communication from 1979 to 2016 proves its increasing institutionalization and internationalization as demonstrated by an upward trend in the papers reflecting cross-institutional collaboration and the diversity of countries of authors [24].

The emerging institutionalization of collaborative university-industry networks in Russia is explored by using conceptual perspectives from institutional theory such as drawing on arguments from strategic choice, network-building, and network failure studies [25].

The present study demonstrates the capacities of the constellations of scientometric indicators purposefully used for integrated assessment of science institutionalization under the conditions of internationalization in this rapidly advancing field. Obviously, the application of the complex methodology of analysis of the mutually linked aspects of institutionalization and co-operation of science enables us to establish the role of the detailed affiliation patterns reflected in the abstracted publications. It becomes evident that in cases of narrow problem-oriented institutions, there is not only a very strictly focused disciplinary specialization but also an intensive involvement of researchers along with ideas and methods from other fields. The set of dynamic scientometric distributions of the number of publications and journals containing them abstracted in these four data-bases, countries of their authors and citations in *WoS*, *BIOSIS* and *Scopus* illustrates the intensive dissemination of ideas, methods, and scientific results and the degree of international collaboration in this interdisciplinary research paradigm.

Conclusions

There is a dramatic growth of the world publication output on the applications of colorectal tumor markers for diagnostic, therapeutic and prognostic purposes. This complex scientometric methodology should become more popular in university curricula, especially within the research methodology courses for postgraduate students and young researchers. The constellation of such specific indicators enlarges the capacities of problem-oriented analyses and faces the challenges of the timely identification of the essential patterns of scientific advances in rapidly expanding interdisciplinary topics.

Our own results along with this rich collection of comprehensive factual information are of interest to the coloproctologists from smaller countries, institutional and national science managers and journal editors as well.

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