Research Commentary

TumorBiology

Tumor Biol 2004;25:327–328
DOI: 10.1159/000081402

Received: August 2, 2004
Accepted: August 6, 2004

The Bioinformatic Catalyst in the Kallikrein Family

Phil D. Rye[a] Torgny Stigbrand[b]

[a]Axis-Shield, Oslo, Norway; [b]Department of Immunology, University of Umeå, Umeå, Sweden

Key Words
In silico · Bioinformatics · Kallikreins

Broadly speaking, bioinformatics is simply the application of computers to solve biological problems. In this context, bioinformatics has been around for decades. Although more specific definitions for bioinformatics will vary, the National Center for Biotechnology Information proposed that bioinformatics represents the field of science wherein biology, computer science and information technology merge into a single discipline. An overview of the more commonly used bioinformatic methods and their applications is described elsewhere [1]. Bioinformatics only really came to the fore after the initiation of the human genome project in 1988. This was a driving force in the development of databases to store and compare the huge amount of sequence data that was being generated throughout the 90s. Hand in hand with this burgeoning wealth of data were the essential advances in bioinformatic tools. Together these facilitated the comparison and search analyses required to add predictive clinical value to the data. Nowadays, any traditional approach to analyse this type of data would be like trying to cut down a forest with a hacksaw. Bioinformatics, data mining or the more fashionable term, in silico analyses, represents the only way to make sense of the huge volume of information available. Consequently, articles based solely on bioinformatic or in silico type of analyses are becoming more frequent. Despite the apparent 'plug-and-play' simplicity of the in silico approach, it still requires the same attention to detail as say choosing an appropriate statistical analysis or a 'wet-bench' method. Contamination of database sequences, redundancy, frameshifts and errors in genome annotations are just a few of the problems previously encountered. Some important issues related to these studies are addressed in a review by Altschul et al. [2], but the literature is replete with tips and suggestions for fine tuning data searches for speed and accuracy.

In this issue of *Tumor Biology,* Yousef et al. [3] have performed an impressive bioinformatic analysis on the newly characterized human kallikrein gene *hKLK6*. The same group has contributed significantly to the kallikrein cause in recent years with a number of publications using traditional 'wet' biology [4–9] and they have been able to substantiate many of their assertions in the current in silico study [3]. This group, led by Prof. E.P. Diamandis in Toronto, are no strangers to the bioinformatic approach [10–12]. Using 11 databases, they have examined the gene structure of *KLK6*, extending the clone sequence by comparing overlapping clones (they identified six published mRNA clones for *KLK6*), identified new splice

KARGER

Fax + 41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2004 S. Karger AG, Basel
1010–4283/04/0256–0327$21.00/0

Accessible online at:
www.karger.com/tbi

Phil D. Rye, PhD
Axis-Shield ASA
Ulvenveien 87
NO–0581 Oslo (Norway)
Tel. +47 22 70 07 66, Fax +47 22 70 07 70, E-Mail phil.rye@no.axis-shield.com

variants from 185 EST clones and highlighted differential expression in cancer that, in turn, may be reflected by these new splice variants. The authors show that the mRNA of *KLK6* is clearly up-regulated in ovarian, uterine, head and neck, myeloma, gastrointestinal, pancreas, esophagus, stomach and colon cancers. However, in breast and brain tumors the expression of *KLK6* is down-regulated. Interestingly, their preliminary investigation of species conservation of *KLK6* may point to other functional roles for the gene in myelin turnover. The authors take care to emphasise the need to verify these findings through additional experimental work, particularly in the context of measuring the expression of the active form of *KLK6* in different cancer types. This type of study clearly underlines the power of the in silico approach in saving valuable bench hours and targeting research resources more constructively. It will be interesting to see just how quickly these studies catalyse the identity of new clinically useful cancer markers from the expanding family of kallikreins. Indeed, this is highlighted in a recent review of the biochemical and clinical aspects of the human kallikreins [13].

References

1 Kapetanovic IM, Rosenfeld S, Izmirilian G: Overview of commonly used bioinformatics methods and their applications. Ann N Y Acad Sci 2004;1020:10–21.
2 Altschul SF, Boguski MS, Gish W, Wootton JC: Issues in searching molecular sequence databases. Nat Genet 1994;6:119–129.
3 Yousef GM, Borgoño CA, White NMA, Robb JD, Michael IP, Oikonomopoulou K, Khan S, Diamandis EP: In silico analysis of the human kallikrein gene 6. Tumor Biol 2004;25:282–289.
4 Yousef GM, Diamandis EP: Expanded human tissue kallikrein family – a novel panel of cancer biomarkers. Tumor Biol 2002;23:185–192.
5 Diamandis EP, Borgono CA, Scorilas A, Yousef GM, Harbeck N, Dorn J, Schmalfeldt B, Schmitt M: Immunofluorometric quantification of human kallikrein 5 expression in ovarian cancer cytosols and its association with unfavorable patient prognosis. Tumor Biol 2003; 24:299–309.
6 Kurlender L, et al: Differential expression of a human kallikrein 5 *(KLK5)* splice variant in ovarian and prostate cancer. Tumor Biol 2004; 25:149–156.
7 Yousef GM, et al: Molecular cloning of a new gene which is differentially expressed in breast and prostate cancers. Tumor Biol 2004;25: 122–133.
8 Yousef GM, et al: The kallikrein gene 5 splice variant 2 is a new biomarker for breast and ovarian cancer. Tumor Biol 2004;25:221–227.
9 Ghosh MC, Grass L, Soosipillai A, Sotiropoulou G, Diamandis EP: Human kallikrein 6 degrades extracellular matrix proteins and may enhance the metastatic potential of tumour cells. Tumor Biol 2004;25:193–199.
10 Yousef GM, Borgono CA, Popalis C, Yacoub GM, Polymeris ME, Soosaipillai A, Diamandis EP: In-silico analysis of kallikrein gene expression in pancreatic and colon cancers. Anticancer Res 2004;24:43–51.
11 Yousef GM, Yacoub GM, Polymeris ME, Popalis C, Soosaipillai A, Diamandis EP: Kallikrein gene downregulation in breast cancer. Br J Cancer 2004;90:167–172.
12 Yousef GM, Polymeris ME, Yacoub GM, Scorilas A, Soosaipillai A, Popalis C, Fracchioli S, Katsaros D, Diamandis EP: Parallel overexpression of seven kallikrein genes in ovarian cancer. Cancer Res 2003;63:2223–2227.
13 Borgono CA, Michael IP, Diamandis EP: Human tissue kallikreins: Physiologic roles and applications in cancer. Mol Cancer Res 2004;2: 257–280.