and AICARFT) observed from *in vitro* to clinical situations *in vivo*. Preliminary efforts in this area have already begun in several laboratories and these are mentioned in chapter 13, which might stimulate additional reading on this subject. The book has placed emphasis on the design and development of therapeutic entities that act against the folate-dependent enzymes, TS and GARFT. Although these antifolates represent the newest drugs under development, the book fails to address the investigations pertaining to the development of inhibitors of other folate-dependent enzymes such as AICARFT, folylpolyglutamate synthetase (FPGS) and folylpolyglutamate hydrolase (FPGH). Furthermore, the chapter on fluoropyrimidines might have been more appropriate in a book dealing with pyrimidine antimetabolites rather than antifolates.

The chapters on thymineless death and genetic determinants demonstrate the importance of how antifolate-induced DNA damage triggers molecular events that initiate cell death through apoptosis, and highlights the important involvement of p53 tumor suppressor gene in this process within the current framework of available knowledge and data. These chapters also provide extremely useful reading when attempting to understand the underlying molecular mechanisms of cytostatic versus cytotoxic effects of antifolate antimetabolites.

Conclusion

Despite the existence of several excellent reviews, a textbook that addresses the theory, rationale, and biochemical and clinical pharmacology of newer antifolates has not yet been available. The present title fulfills this gap at the appropriate time by providing a base for stimulating, innovative and utilitarian research in antifolates. This book is highly recommended and is essential reading for advanced students, medicinal chemists, pharmacologists and oncologists.

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Enhancing information sharing

It currently takes 10–12 years for a new drug to reach the market. However, once the patent has expired on the new drug entity, the company loses most of the revenue on that particular drug. It has been estimated that for every extra day taken in the development stage, the company loses an average of $1 million [*The Delphi Report on Knowledge Management* (1997) Delphi Consulting Group]. One important aspect of getting a drug to the market quickly is teamwork. In the pharmaceutical and biotechnology industries, this teamwork involves several different groups of workers, often between many different global sites. Xerox (Stamford, CT, USA) have devised a number of packages designed to save time during the drug discovery and development processes, registration and packaging [Lawrence, R.N. (1999) *Pharm. Sci. Technol. Today* 2, 390–391]. The company say these packages enable access to current knowledge (AskOnce™), distributing and sharing it between the different groups (DocuShare™) and monitoring the information (Eureka™).

Accessing knowledge

Throughout the drug discovery process, it is essential to remain aware of any similar research being carried out by other companies so that an early decision can be made whether to proceed with the research. However, such information is often indexed, catalogued and stored in numerous databases, both externally on the Internet and internally, and can only be accessed by using a combination of different methods. AskOnce is a query package that searches several Web search engines (e.g. AltaVista, Excite), Web databases (e.g. the US Patent Office), legacy databases (e.g. Oracle), document repositories (e.g. Documentum, DocuShare) and groupware (e.g. Lotus Notes, Microsoft Exchange) simultaneously in one query. This therefore reduces the number of different searches necessary and eliminates the need to combine the results of several different searches. New links to databases and search engines can be created, queries can search non-indexed information to view the most up-to-date information and it can be set to run continually so that any emerging relevant information is immediately highlighted.

A query can also be translated into the language of the database that it is programmed to search. Furthermore, the package has been designed to reduce the number of hits returned, being reported to compress the output of these queries by up to ten-fold. The results of the queries are expressed in a common format, and to simplify examination of the output, instant summaries of documents can be produced (5–6 sentences in the required language)

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through searching for certain words or expressions.

Distributing knowledge

Only 58% of an organization's knowledge is documented and out of this, only 12% is in a knowledge base that is technological accessible to others, the other 46% being stored at numerous sites either electronically or on paper [*The Delphi Report on Knowledge Management* (1997) Delphi Consulting Group]. DocuShare has therefore been produced to scan information held on paper documents directly either onto a PC, into e-mail (e.g. into public folders) onto the Internet, or into electronic document management systems to enable the immediate sharing of the information between different groups of workers.

Monitoring knowledge

Further sources of valuable information include workers, whose experiential knowledge is often lost when they either leave a company or retire (up to 42%) [*The Delphi Report on Knowledge Management* (1997) Delphi Consulting Group]. One way of trying to retain this knowledge base for use by others has been to encourage workers to input this information into an electronic database as they use or gain it. This is the idea behind Eureka, which involves the authoring of 'tips', followed by their validation by a respected group of peers, so that they can be shared and used by other workers in the organization. These tips can be submitted as text, graphics or sound and then validated by a trusted expert. To encourage workers to add their tips to the database, they, and the validators, get their name ascribed to the tip, making them the contact person for any related queries and promoting their name as contributors across the Web.

Rebecca N. Lawrence

Lawsuits…

The US District Court for the Northern District of California has ruled that **Roche Molecular Systems** and **Roche Diagnostics Systems** (Basel, Switzerland) do not have express or implied licence rights to the hepatitis C virus (HCV) technology owned by **Chiron Corporation** (Emeryville, CA, USA). It was alleged that Roche was infringing certain Chiron US patents concerning the use of polynucleotides for nucleic acid testing (NAT) that detect HCV in the blood, and might be used in the future to improve the accuracy of HCV and HIV testing in donated blood. Roche unsuccessfully claimed that it had obtained a licence to use this technology through the sale of Cetus Corporation's NAT business to Roche. The final decision, which is subject to appeal, was the result of cross-motions for summary judgement filed by the parties in connection with the ongoing patent infringement litigation in the US. Roche has requested reconsideration of portions of the decision.

US patents for reverse transcriptase enzymes used in the cloning of cDNA molecules (US5244797 and US5668005), which had been assigned to **Life Technologies** (Rockville, MD, USA), have been ruled to be unenforceable by the US District Court of the District of Maryland, because of a breach of the company's duty of candor to the US Patent and Trademark Office (PTO). This company had originally sued **Clontech Laboratories** (Palo Alto, CA, USA) for infringement of these patents, as well as for breach of label licence agreements. The ruling was made in Clontech's favour as the court rendered that the patent applicants and their representatives had intentionally withheld material information and had made affirmative misrepresentations to the PTO examiner.

Gensia Sicor Pharmaceuticals (Irvine, CA, USA) has entered into a settlement agreement with **Protocol Systems Inc.** (Warrington, PA, USA) regarding a complaint by Protocol that a development and supply contract that provided for the purchase of a device to be used by Gensia Automedics' GenESA® Systems was breached. As the settlement was within the liability provision recorded by Sicor in the fourth quarter of 1998, it will not result in any further earnings for the company.