metabolizes >50% of human drugs, and ligands for the nuclear xenobiotic receptor PXR seem to share key but enigmatic structural similarities. Not all targets to be avoided are drug metabolism proteins, however. Ekins also outlines efforts to understand why an array of structurally-distinct compounds can block the human ether-a-gogo cardiac channels (hERG), which causes potentially lethal long-QT cardiac syndromes in some patients.

Flexibility

A small number of generalities about molecular promiscuity has emerged. Most promiscuous proteins use a combination of hydrophobic and hydrogen-bonding interactions to bind to substrates and ligands, but most of these proteins are also highly flexible. This flexibility is particularly difficult to handle, as it adds tremendous complexity to the problem of *in silico* modeling of lead compound behavior.

One thing is clear: predicting the lability of compounds in humans is of critical importance to the use of current drugs, the development of new ones, and the potential for tailoring clinical regimen to individuals.

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Obituary of Dr Paul Janssen (1926-2003)

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Dr Paul Janssen passed away on November 11 last year while attending a conference in Rome. He died as he had wished to, suddenly and in the line of his work. He leaves behind a wife, five children and thirteen grandchildren. In the annals of medicinal chemistry he will be remembered as one of the greatest drug designers of all times. His track record is most impressive: 77 original medicines brought to the market and several more awaiting further development, over 850 scientific publications, more than 100 patents registered in his name, 22 honorary doctorates and a score of scientific and civil distinctions and awards. In 1953 he founded a research laboratory that became world famous for its inventiveness and productivity. During the past 50 years Janssen Pharmaceutica, acquired in 1961 by Johnson and Johnson, evolved into a multinational company in its own right, employing about 25,000 people in 43 subsidiaries spread over five continents.

Paul Janssen's major achievements are in the fields of analgesics, psychotropics,

anthelmintics, antimycotics, antihistaminics and gastro-intestinal compounds. He has saved millions of human lives and improved the quality of life of countless people. Five Janssen compounds have been included in the list of essential medicines of the World Health Organization. His products also found application in veterinary medicine, agriculture and material protection.

Many visitors to the Janssen laboratory have often wondered what might have been the key to its success. It certainly could not be found in the buildings and facilities, which were rather austere. Nor did it show in the laboratory equipment, which was home made to a great extent. Many of the initial researchers were self-made persons, often lacking extensive academic qualifications. To a large extent, the success of the laboratory can be attributed to the character and personality of Paul Janssen. He possessed a rare combination of talents, which made him a gifted pharmacologist and chemist, a compassionate clinician and an alert entrepreneur. He possessed the charisma to inspire his collaborators and make them feel part of an enterprise that gave meaning to their life. All addressed him affectionately as Dr. Paul. His memory was legendary, and so was his faculty to discern rapidly between what is important and what is not for bringing new and better medicines to

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patients. By virtue of perseverance and confidence, success became a habit. He possessed a great capacity for work and a universal interest in matters of science, history, philosophy, languages and art. He played the piano well. In summary, apart from being a great scientist, he was a man for many seasons, a humanist and Renaissance man.

Paul Janssen will also be remembered by those who have accompanied him on his scientific Odyssey for his unique concept of organizing research, or rather for his peculiar way of not organizing what should be left to emerge and flourish on its own accord. From the beginning his research laboratory was centered around competent people. Rather than have a pyramidal reporting system and division of work into fixed processes, he preferred a flat and organic structure. Activities within the laboratory depended strongly on the presence or arrival of individuals. He gave maximal freedom to those he trusted for their competence and loyalty to the common goal, which was to discover new drugs for important diseases within their field of expertise. He expected his collaborators to constantly think of interesting plans and ideas. The best part of his working day was spent in discussions with his collaborators, be they key scientists or laboratory technicians. Invariably his first question was "What's new? He constantly scanned the scientific literature for articles that might be of interest for one or the other of his collaborators, who then were expected to review and discuss the subjects with him. As a rule, intellectual authority was severely rejected. Nothing was to be assumed and critical questioning was a continuous exercise. His scientific method could be termed as Socratic. The purpose of discussion and criticism always was to learn, never to persuade or to judge. His constant concern was to find out what was credible and what was valuable, doing away with everything that appeared unfounded or useless. Dr. Paul liked to think of his own role in the laboratory as that of the conductor of an orchestra. He strongly believed that professional and competent players need only a minimum of direction and coordination in order to achieve a harmonious and effective interplay.

Paul Janssen's concept of organizing drug design around competent people and critical questioning has resulted over a period of 50 years into an incredible wealth of new medicines. Many of them have revolutionized medical practice. We need only think of fentanyl and sufentanil in analgesia, haloperidol and risperidone in psychiatry, levamisole and mebendazole against parasitosis, miconazole and itraconazole in mycoses, diphenoxylate and loperamide for the treatment of diarrhoea, the gastroprokinetic domperidone, the antihistaminic astemizole, and many others. After retiring from his official functions and until the last moment of his life, Paul Janssen continued doing research at his Center for Molecular Design. Here with a small and dedicated staff and with the help of reputed scientists from all corners of the world he designed new drugs for the treatment of HIV/AIDS. Unfortunately, he did not live to see the fruit of his work in the form of essential medicines that are so dearly needed to combat the worst scourge of our time. There is no better way to honor his memory than to continue and finish the voyage that he undertook.

Erratum

In the 1st April 2004 issue of *Drug Discovery Today* (Vol. 9, No. 7, p. 298), in the article entitled *New rotavirus vaccine could be licensed this year*, it was incorrectly stated that roataviruses are protozoan parasites. The first subheading should have been *RNA viruses* and the subsequent text should have read: 'Rotaviruses are common RNA viruses that cause potentially fatal diarrhoeal illness in children.'

The Editorial team would like to apologize for any confusion that this might have caused.

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