The SCE enigma

Charles H. Ockey

Sister Chromatid Exchange. Edited by Avery A. Sandberg. Pp.706. ISBN 0-8451-2401-3. (Alan R. Liss: 1982.) £74, \$134. *Sister Chromatid Exchange*. Edited by Sheldon Wolff. Pp.306. ISBN 0-471-05987-0. (Wiley: 1982.) £58.20, \$93.10.

IN 1957 J.H. Taylor first demonstrated the phenomenon of sister-chromatid exchange (SCE). Taylor's studies, however, were limited by the poor resolution of ³H-thymidine autoradiography. It was not until 15 years later, and the advent of detection techniques involving differential staining (or fluorescing) of chromatids following uni- and bi-filarly substitution by 5-bromodeoxyuridine, that further progress was made in SCE research.

Using these new techniques it was soon discovered that many known mutagenic and carcinogenic agents increased SCE yields at concentrations 10–100-fold lower than those required to induce other genetical events. Moderate increases in SCEs did not, however, appear to produce any serious perturbations in the cells. These findings suggested that an SCE test would be of great value in discovering even weak genotoxic agents in the environment.

After eight years of intensive research, much of which is documented in the books under review, it may seem surprising that the biological significance and mechanism of induction of SCEs still remain a mystery. Much of the work during this period has concentrated on the relationships between SCE induction and other genetic changes involving the processes of mutation, carcinogenesis, chromosome breakage, meiotic recombination and DNA repair mechanisms. SCEs, however, do not appear to be definitely related to any one of these processes. They are an "S dependent" event induced at the replicating fork as it passes through, or is delayed at, some as yet undefined perturbation or lesion in the DNA helix, possibly at the junctions of adjacent replicons or replicon clusters.

The reader of either of these books may also be astonished at the degree to which the various results in this area conflict. For example, the yield of SCEs in peripheral lymphocytes taken from smokers has been found to be either increased, or to remain unaffected; the co-carcinogen, TPA, was found to be an effective SCE inducer by some groups but not by others; and cells from the cancer-prone Bloom's syndrome, which usually manifest a high spontaneous SCE level when grown in the presence of normal cells, have been shown to increase the SCEs in normal cells, while other evidence indicates that the presence of normal cells reduces the SCE levels in the Bloom's cells.

These differences do not necessarily reflect "bad science"; rather, they are a

result of our lack of basic knowledge of the SCE mechanism and the various external factors which influence SCE induction. Some of these factors are discussed in parallel chapters in the two books, particularly in connection with the baseline variation in SCE frequencies in control peripheral blood cultures — SCE induction is very sensitive to environmental conditions during the culture process and is also dependent on the state of health of the lymphocyte donor.

Two other important factors controlling SCE levels, including those in fibroblast cultures and probably *in vivo*, are the time of cell fixation after 5-bromodeoxyuridine incorporation and the concentrations of 5-bromodeoxyuridine used to demonstrate SCEs. The influence of fixation time is still not clear and, again, the results support different conclusions. The other factor, 5-bromodeoxyuridine concentration (abbreviated to BrdU in Sandberg, but to BrdUrd in Wolff) has been used at levels ranging from 0.3 to 200 g/ml. As discussed in both books, BrdU itself is a mutagenic agent which induces SCEs, and as it is required to detect SCEs the presence or absence of a "spontaneous" level still remains a matter for debate. Since these volumes went to press, however, we have been able to show in both peripheral lymphocytes and Chinese hamster fibroblasts that increasing levels of BrdU incorporated into the DNA seriously reduce the expression of SCE lesions in cells treated with certain mutagenic agents. There are also results quoted in both volumes to indicate that the BrdU in the medium has a greater effect on SCE induction than that incorporated into the DNA. As is suggested by authors in each of the books, some form of standardization is required before the SCE method becomes a more reliable weapon in the armoury of tests for genetic hazards in the environment.

The two volumes cover approximately the same general areas of SCE research, and although Wolff contains a more comprehensive index, there are some topics which have been omitted or which are dealt with only in brief. The current theories accounting for SCE induction mechanisms are described by their respective proponents in Sandberg, and this book also includes a lucid chapter discussing the merits of these and other theories. There is some degree of repetition of material both within and between the two volumes, but this is not altogether unsatisfactory; author bias is reduced and the reader is exposed to a healthy mix of controversy and speculation. As to readership, Wolff, the shorter book, covers the most important facets of SCE research and is especially recommended to general and medical readers. Sandberg embraces a broader area and includes more details of experimental test systems, a wider series of test systems and list of drugs tested for SCE induction. This book would therefore be particularly

appreciated by scientists and industrialists.

Between them the two volumes contribute much to our knowledge of this complex yet fascinating corner of biological research. Their publication at this time is opportune, and it is to be hoped that their appearance will encourage further research into unravelling the SCE enigma. □

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Naturalist from the Purple Land

Wynford Vaughan-Thomas

W.H. Hudson: A Biography. By Ruth Tomalin. Pp.314. ISBN 0-571-10599-8. (Faber & Faber/Faber Inc.: 1982.) £13.50, \$19.95.

How does the reputation of W.H. Hudson stand today? I suppose that he is a somewhat shadowy figure even to well-informed readers who are keen naturalists. Things were different in the early days of this century. Hudson had become almost a cult figure, the very symbol of freedom and escape in a land where expanding industry was eroding the last traces of the old rural England. Arnold Bennett, then the arbiter of popular literary taste, declared, "How many men know England — the actual earth and flesh of England — as Mr Hudson knows it?"

But the curious fact remains that the man hailed as the authority on the soul of the English countryside never saw it until he was thirty, was the son of an American mother and a father who was half Irish and had spent the whole of his early life on the wide pampas of South America. It was the quarter-Devonian blood that eventually prevailed.

Hudson's early free-ranging life on the pampas, then unfenced and alive with vast flocks of exotic birds, made him an ornithologist — or as he always preferred to call himself, a field naturalist. He gained a well-deserved reputation as a collector of specimens for the Smithsonian Institute in Washington and the Zoological Society of London. Ruth Tomalin has unearthed a photograph of the young Hudson, which shows him as a strikingly handsome man; no wonder his admirers saw him as a "caged eagle" when he eventually settled in London. He found London tough going, and only saved himself from near destitution by marrying his landlady. He was devastatingly honest about his marriage in later years: "Now I was never in love with my wife or she with me, but we became good friends". Emily Hudson was more than a good friend. She believed in